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Reyna María Ocegueda Estrada

Use of topical oxygen therapy to optimize postoperative healing of oral surgical wounds after dental implant placement

CURITIBA
2024

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Dissertação apresentada a Faculdade ILAPEO como parte dos requisitos para obtenção de título de Mestre em Odontologia com área de concentração em Implantodontia

Orientador(a): Prof. Dr. Tatiana Miranda Deliberador

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Aprovada em: 06/04/2024

Dedicatória

Com el deseo de participar com um granito de arena al desarollo y estudio de la Odontogía, dedicado a mis maestros y colegas estudiantes, a todos aquellos con el gusto de estudiar y trabajar en pro del crecimiento de esta profesión.

Agradecimentos

Agradezco a la fuente, de la que emana la creación misma de todo lo que existe, por abrir los caminos , a mi familia por el impulso y soporte, a mis maestros por la inspiración que sembraron en mi, en especial a mi profesora orientadora dra. Tatiana Deliberador por su enseñanza, ayuda y compromiso, a mis compañeros por las experiencias vividas.

Sumário

1. Artigo científico 1

Artigo de acordo com as normas da Faculdade ILAPEO, para futura publicação no periódico **Case Reports in Dentistry**

USE OF TOPICAL OXYGEN THERAPY TO OPTIMIZE POSTOPERATIVE HEALING OF ORAL SURGICAL WOUNDS AFTER DENTAL IMPLANT PLACEMENT.

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RESUMO

Próteses implanto-suportadas tornaram-se uma alternativa comum para o tratamento de pacientes edêntulos totais ou parciais com bons resultados a longo prazo. A cicatrização rápida e eficaz de feridas cirúrgicas contribuirá para este propósito. O objetivo deste relato de caso foi avaliar por observação clínica o efeito do gel oral com oxigênio ativo (blue®m) na cicatrização de feridas bucais pós-cirúrgicas após colocação de implante dentário. Dois pacientes foram submetidos à cirurgia de colocação de implantes dentários por técnicas abertas convencionais para avaliar a cicatrização de feridas pós-cirúrgicas associada a carga imediata. No primeiro paciente, foi realizada cirurgia de arcada completa com quatro implantes e redução óssea. No segundo, foram colocados dois implantes unitários inferiores nos sítios 46 e 36 com carga imediata e prótese provisória. O gel de oxigênio ativo (blue®m) foi colocado nos tecidos antes do fechamento do retalho e após a sutura. Os pacientes foram orientados a colocar o produto apenas no lado direito três vezes ao dia e nenhum produto ou medicamento tópico no lado esquerdo. Comparações observacionais foram feitas pelo Índice de Cicatrização Precoce de Feridas (EHI) aos 7, 15 e 30 dias pós-operatório no arco completo, e 3, 7, 10, 15, 30 e 60 dias nos casos únicos. Como resultado da observação por comparação em ambos os casos clínicos, sugere-se a utilização de oxigênio ativo em gel oral (blue®m) como antisséptico e agente estimulador de cicatrização de feridas cirúrgicas orais. É indicado como uma alternativa confiável e segura para o cuidado pós-cirúrgico de feridas bucais após a colocação de implantes dentários, nestes casos clínicos otimizou a cicatrização de feridas. Estudos são necessários para apoiar esta sugestão.

Palavras-chave: Oxigenoterapia tópica; Cicatrização de feridas orais; Implantes dentários.

ABSTRACT

Implant-supported and implant-borne prostheses have become a common alternative for treating total or partial edentulous patients with good long-term results. Prompt and effective healing of surgical wounds will contribute to this purpose. The objective of this case report was to evaluate by clinical observation the effect of oral gel with active oxygen (blue®m) on the healing of oral post-surgical wounds following dental implant placement. Two patients underwent dental implant placement surgery by conventional open techniques to evaluate the healing of post-surgical wounds subjected to flaps, both with immediate loading and provisional. In the first one, a full arch surgery with four implants and bone reduction was performed. In the second, two mandibular single implants were placed in sites 46 and 36 with immediate loading and provisional. The active oxygen gel product (blue®m) was placed in the tissues before closing the flap and after suturing. Patients were instructed to place the product only on the right side three times a day and no product or topical medication on the left side. Observational comparisons were made by Early Wound Healing Index (EHI) at 7, 15, and 30-days post-surgery in the complete arch, and 3, 7, 10, 15, 30, and 60-days in the single cases. As a result of the observation by comparison in both clinical cases, it is suggested that the use of active oxygen in oral gel (blue®m) as an antiseptic and stimulate agent of healing to surgical oral wounds. Is indicate a reliable and safe alternative for the post-surgical care of oral wounds after the placement of dental implants, in these clinical cases it optimized wound healing. Studies are required to support this suggestion.

Keywords: Topical oxygen therapy; Oral wound healing; Dental implants.

INTRODUCTION

Treatment with Osseo integrated dental implants is a predictable and widespread treatment alternative to omit the need for fixed dentures or removable prostheses in the rehabilitation of edentulous patients with predictable short- and long-term success rates [1]. The factors that determine the success and survival of implants are related to the host, the implant, the prosthesis, and the surgery [2]. In this last point, the healing of the surgical wound will reestablish the protection barrier against pathogenic invaders, mechanical stresses, and physical trauma [3]. Four consecutive stages of tissue change occur in this healing: hemostasis, inflammation, proliferation, and remodeling. Hemostasis and inflammation will begin from the time of injury and continue for up to four to six days. The proliferation stage means re-epithelialization, angiogenesis, granulation tissue formation, and collagen deposition. This phase starts from day four and will last up to three weeks after a soft tissue injury. The soft and/or hard tissue remodeling phase will continue for approximately one year [4]. Wound healing in the mouth is driven by the inflammatory and vascular response, at this point angiogenesis or neovascularization plays a significant role. Capillary growth is necessary for

optimal wound healing by providing oxygen and micronutrients and removing catabolic waste products from the healing tissues [5].

Therapeutic approaches aimed at improving tissue oxygenation may be the key to success in wound management [6]. Oxygen is an essential element for the maintenance of healthy tissues and for wound healing processes [7]. Hypoxia in the wound is natural in tissue injury, it requires energy and balance in oxygen production for neovascularization and epithelialization [3,7]. Hyperbaric oxygen therapy and topical oxygen have been reported to improve wound healing [6]. Other means promote angiogenesis in oral wound healing during the proliferation process, such as ultrasound, lasers, platelet-rich plasma (PRP)/platelet-rich fibrin (PRF), and various chemical agents such as hyaluronic acid, anthoxanthin and Centella asiatica. These include cutting-edge therapies such as the use of growth factors, bioengineered skin substitutes, and stem cell therapy [3].

There is currently a product on the market focused on the principle of improving topical oxygen delivery to wounds oral care (blue®m). This easy-to-use product seems to positively influence tissue healing by improving oxygenation without risking the stability of the microbiome. The slow and continuous release of oxygen in (blue®m) in the tissues arises from the components present in the formula honey (glucose oxidase enzyme) and sodium perborate. When these ingredients meet tissue fluids, they are transformed into hydrogen peroxide (H_2O_2) at low concentrations (0.003 to 0.15%). The oral gel is the product with the highest amount of oxygen release, thus its healing and bactericidal actions [3,8].

The objective of this case report was to evaluate by clinical observation the effect of oral gel with active oxygen (blue®m) on the healing of oral post-surgical wounds following dental implant placement.

Case Presentation

Diagnosis and Treatment Plan:

Patient one

A 74-year-old female patient, systemically healthy, came to the clinic with the need to change her lower removable prosthesis for a fixed treatment option to improve her functionality. The upper dental arch had a fixed prosthesis on teeth and the lower arch had a Kennedy class I with only three remaining teeth on the left side (Figure 1).

After a comprehensive clinical and tomographic examination (Figure 2), the treatment plan consisted of performing a full arch protocol on four mandibular implants with provisional

and immediate loading, (Neo Arch technique Neodent®) with vertical bone reduction, and conventional open surgical technique to evaluate healing in wide wounds. The oral gel with active oxygen release (blue®m) was placed on the implants and right surgical site before and after flap closure and the patient placed the gel three times a day only on the right side during the evolution of the wound (clinical observation were made at 7, 15, and 30-days post-surgery) to compare the healing with the left side where no topical product or medication was indicated.

Patient two.

A systemically healthy 67-year-old female patient came for a consultation to have fixed prosthetic teeth in edentulous sites 46 and 36 after her diagnostic examination and evaluation of her initial situation (Figure 3). After a comprehensive clinical and tomographic examination (Figure 4), the treatment plan consisted of placing two osseointegrated dental implants in these sites with provisional and immediate loading. Placed with conventional freehand surgery to evaluate the healing after wounds with flaps.

The active oxygen extended-release gel (blue®m) was placed on the implant and right surgical site before and after flap closure and the patient placed the gel topically three times a day only on the right side during the evolution of the wound (clinical observation were made at 3, 7, 10, 15, 30 and 60-days post-surgery) to compare the healing with the left side where no topical product or medication was indicated.

Surgical procedure:

All surgical procedures were performed by the same operator.

Patient one

The surgical procedure was started with asepsis and antisepsis, and local anesthesia was administered right and left mandibular regional block with mepivacaine-epinephrine 36 mg/ 0.018 mg 1.8 ml (Scandonest 2% Special France Septodont.). Exodontia was performed on teeth 33, 34, and 35. An incision was made along the entire alveolar ridge in an extension equivalent to the site from the right first molar to the left first molar with two posterior vestibular discharges using a scalpel blade 15c.

A full-thickness flap was displaced confirming the seating of the multifunctional guide (Figure 5a). The predetermined osteotomy was performed with surgical gouges and drills and the emergence of the right and left mental nerves was visually located and marked with sterile graphite (Figure 5b). The complete drilling sequence for the posterior implants was performed,

the emergences were designed at the level of the second premolars, and the posterior implants were placed with an inclination of approximately 17 degrees (Figure 5 c-d).

The implants were installed according to the manufacturer's recommendations (HELIX GM ACQUA, Neodent®, Curitiba/PR, Brazil). All implants achieved torque of more than 32 Ncm. The trans-mucosal prosthetic attachments were then placed as follows. A conical angulated conical minipilar GM exact 17 degrees Neodent® on the right and left posterior implants with a torque of 20 Ncm. A minipilar conical GM Neodent® on the right and left anterior implants with a torque of 32 Ncm.

Active oxygen gel (blue®m) was placed on the surgical site in the right implants (Figure 6a), and the wound synthesis was performed, eight single stitches were made until total closure was achieved using 4-0 nylon. The maneuvers for the capture and adjustment of the provisional denture were immediately performed on four temporary titanium cylinders for the GM mini conical abutment (Figure 6b). Before placing the provisional prosthesis already adjusted and polished, active oxygen gel (blue®m) was placed again on the wound already sutured on the right side (Figure 6c).

The patient was prescribed the antibiotic amoxicillin/clavulanic acid 875/125 mg every 12 hours for 7 days and ibuprofen 400 mg every 8 hours for 3 days.

As part of the post-surgical instructions, the patient was instructed to apply active oxygen gel (blue®m) three times a day only on the wound on the right side, applying it on the vestibular and lingual side until it was placed on the right wound every day until the end of the wound healing follow-up (Figure 6d).

Patient two

The surgical procedure was started with asepsis and antisepsis, and local anesthesia was administered right and left mandibular regional block with mepivacaine-epinephrine 36 mg/ 0.018 mg 1.8 ml (Scandonest 2% Special France Septodont). Surgery on the right and left sides were performed on the same day by the same operator.

In the left side an incision was made through the alveolar ridge corresponding to site 36, now edentulous and sulcular to the proximal face of the neighboring teeth. A full-thickness flap was reflected, and a drilling sequence was performed up to drill 3.5. It was an area with the medullary bone of low density, a HELIX GM ACQUA 3.75x10 mm (Neodent®, Curitiba/PR, Brazil) implant was placed, as well as an intraosseous placement of 2mm to the vestibular crest (Figure 7a) with a torque of 32 Ncm. A universal click GM exact 4.5x4x3.5

universal stem (Neodent®, Curitiba/PR, Brazil) was installed with a torque of 20 Ncm (Figure 7b). The wound was sutured with stitches at the level of the proximal papillae with polyglactin 910 4-0, and a temporary prosthesis was placed (Figure 7c) in sub occlusion without cement using the temporary click cylinder of the GM universal stump system. Immediate periapical x-ray was performed to verify the correct position of the implant and adaptation of the prosthetic component (Figure 7d).

In the right side an incision was made along the entire alveolar ridge corresponding to site 46, now edentulous and sulcular to the proximal face of the neighboring teeth. A full-thickness flap was reflected, and a complete drilling sequence was performed, a HELIX GM ACQUA 4.3x10 mm (Neodent®, Curitiba/PR, Brazil) implant was placed. Intraosseous placement 2.5mm to the vestibular ridge with a torque of 32 Ncm. A universal click GM exact 4.5x4x3.5 universal stem with 20 Ncm torque was installed (Neodent®, Curitiba/PR, Brazil) (Figure 8a), after was apllied active oxygen gel (blue®m) was then placed in the surgical area (Figure 8b). The wound was sutured with stitches at the level of the proximal papillae with polyglactin 910 4-0, and a temporary prosthesis was placed in sub occlusion (Figure 8c) Immediate periapical x-ray was performed to verify the correct position of the implant and adaptation of the prosthetic component (Figure 8d). At the end of the surgery, the oral gel with active oxygen was applied again.

The patient was prescribed oral antibiotic amoxicillin 500 mg every 8 hours for 7 days and ibuprofen 400 mg every 8 hours for 3 days. As post-surgical indications, the patient was asked to apply active oxygen gel (blue®m) three times a day (8/8hours) only on the wound on the right side, applying it on the vestibular and lingual side every day until the end of the healing follow-up.

Monitoring of healing, observation, and recording of data using the Early Wound Healing Index (EHI) [9]:

Postoperative healing was assessed by an EHI differentiating between 5 different degrees as described below.
1: complete flap closure – no fibrin line in the interproximal area
2: complete flap closure – fine fibrin line in the interproximal area
3: complete flap closure – fibrin clot in the interproximal area
4: incomplete flap closure – partial necrosis of the interproximal tissue
5: incomplete flap closure – complete necrosis of the interproximal tissue

Patient one

Clinical observational with EHI was made at 7, 15, and 30-days post-surgery both on the right and left side (Table 1). The patient received the oral gel with active oxygen only on the right side of surgery.

On postoperative day seven (Figure 9), on the right side, an Index 2 (EHI) with total closure of the flap and the presence fine fibrin line in the interproximal area (Figure 9b-c). On the left side, an Index 3 (EHI) was determined with total closure of the flap with the presence of more fibrin clots along the wound and bleeding points (Figure 9b-d).

On the fifteenth day after surgery the right side shows better healing than the left side (Figure 10a-b). The right side shows an Index 1 (EHI) total flap closure without fibrin zones (Figure 10b) and the left side shows an Index 2 (EHI) total flap closure with thin fibrin zones (Figure 10b).

On the thirtieth postoperative day, shows similar healing process between the right and left side. However, the right side where the oral gel was applied shows a smaller healing line (Figure 11a-b). The right side shows an Index 1 (EHI) with total flap closure without fibrin areas (Figure 11b), and the left side shows an Index 2 (EHI) with total flap closure, fine fibrin lines in the posterior area of the wound, and still noticeable wound edges. (Figure 11b).

Patient two

Clinical observational with EHI was made at 3, 7, 10, 15, 30, and 60-days post-surgery both on the right (buccal and lingual) and left side (buccal and lingual) (Table 2). The patient received the oral gel with active oxygen only on the right side of surgery.

On day three post-surgery, on the right side an Index 2 (EHI) was observed on the vestibular (Figure 12a) and lingual (Figure 12b) side with total flap closure and a fibrin line in the interproximal region. On the left side an Index 2 (EHI) was observed on the vestibular side with total flap closure and a cervical fibrin line (Figure 12c) and on the lingual side an Index 3 (EHI) was observed with not total flap closure and wide fibrin clots marginal to the crown (Figure 12d).

On day seven post-surgery, on the right side (Figure 13a-b), an Index 1 (EHI) was observed on the vestibular side with total closure of the flap and no fibrin line in the interproximal area and marginal region (Figure 13a), and on the lingual side an Index 2 (EHI) was observed with total closure of the flap and a fine fibrin line in the marginal region (Figure 13b). On the left side (Figure 13c-d), an Index 2 (EHI) was observed on the vestibular side with total flap closure and a cervical and interproximal fibrin line (Figure 13c), and on the lingual

side an Index 3 (EHI) was observed with total flap closure and wide fibrin clots marginal to the crown and interproximal region (Figure 13d). It is clear from clinical observation that the right side showed better healing than the left side.

On postoperative day ten, on the right side (Figure 14a-b), an Index 1 (EHI) was observed on the vestibular and lingual side with total flap closure and no fibrin line in the interproximal area and marginal region. On the left side (Figure 14c-d) an Index 2 (EHI) was observed on the vestibular and lingual side with total flap closure and a cervical fibrin line. Through clinical observation, it is clear, mainly on the lingual side, that the right side showed better healing.

On postoperative day fifteen, better healing was observed on the right side where the oral gel with active oxygen was used. On the right side (Figure 15a-b), an Index 1 (EHI) was observed on the vestibular and lingual side with total flap closure without fibrin. On the left side (Figure 15c-d), an Index 2 (EHI) was observed on the vestibular and lingual side with total flap closure and an interproximal fibrin line.

On postoperative day thirty, on the right side (Figure 16a-b), an Index 1 (EHI) was observed on the vestibular and lingual side with total flap closure without fibrin. On the left side (Figure 16c-d), an Index 2 (EHI) was observed on the vestibular and lingual side with total closure of the flap and fibrin line marginal to the crown. The presence of inflammation was observed due to bacterial biofilm in vestibular side.

On day sixty post-surgery, on the right side (Figure 17a-b), an Index 1 (EHI) is observed on the vestibular and lingual side with total flap closure without fibrin. Excellent healing is observed in the region of the cervical margin and the region of the mesial and distal papillae. On the left side (Figure 17c-d), an Index 2 (EHI) was observed on the vestibular side. It was observed complete closure of the flap with incomplete formation of the distal papillae (Figure 17c), and on the lingual side, an Index 1 (EHI) was observed with complete closure of the flap (Figure 17d).

At all post-operative times, the right side showed a better healing process compared to the left side where the oral gel with active oxygen release was not applied.

Table 1. Clinical observational with EHI in 7, 15, 30-days post-surgery on right and left side in the patient one.

Postoperative Day.	EHI Right side	EHI Left Side
7 days	2	3
15 days	1	2
30 days	1	2

Table 2. Clinical observational with EHI in 3, 7, 15, 30 and 60-days post-surgery on right and left side in patient two.

Postoperative Day.	EHI Right Buccal Side	EHI Right Lingual Side	EHI Left Buccal Side	EHI Left Lingual Side
3 days	2	2	2	3
7 days	1	2	2	3
10 days	1	1	2	2
15 days	1	1	2	2
30 days	1	1	2	2
60 days	1	1	2	1

Discussion

After implant placement, bacterial control is necessary, since microspaces and infiltration of oral bacteria could lead to colonization in the peri-implant tissues, affecting osseointegration and influencing early implant loss [10]. Wound healing without bacterial intervention is a key point for initial implant success [11]. In parallel, many wound healing processes, such as oxidative destruction of bacteria, re-epithelialization, angiogenesis, and collagen synthesis, depend on oxygen. Topical oxygen application to the wound has been shown to promote healing through various processes, such as antibacterial activities, neovascularization, collagen production, epithelialization, phagocytosis (encompassing microorganisms, cells, or debris by macrophages or neutrophils), and degradation of necrotic wound tissue [12]. Topical oral oxygen therapy (TOOT) aims to activate the healing process by supporting neovascularization, removing toxins, stimulating the formation of new blood cells, increasing stem cell production, and killing bacteria [13]. This can be observed in the clinical cases presented. The side that received topical oxygen therapy showed better healing than the side that did not receive it. In this way, we can suggest that blue®m oral gel led to faster healing, as proven in previously published studies [8].

In this case report, the healing of post-surgical wounds with and without the use of active oxygen gel (blue®m) after dental implant placement was compared by clinical observation and described by an early wound healing index (EHI) described in previous research article [9]. This index not only differs in different degrees of exposure but also records the amount of fibrin formation when complete closure is present. According to the authors [9], clinical experience has shown that the most rapid and uneventful healing is associated with no or minimal fibrin formation, as this occurs when trauma to the surgical site has been reduced to a minimum. This clinical observation could be verified in this clinical case. In patient one, where full-arch surgery was performed, a smaller scar line was present when the active oxygen-releasing gel was used (right side). This suggests that the gel helped stimulate faster healing, with less fibrin formation during this process.

Another important point is that the TOOT with (blue®m) can be a substitute for chlorhexidine (CHX), a safe alternative in post-surgical care actively promoting healing processes and as an antiseptic effectively reducing the microbial load and pain during the postoperative healing period after dental surgery [14]. It is suggested that the use of oral gel may have contributed to less local biofilm accumulation due to its bactericidal action. This can be observed 30 days after surgery. The left side that did not receive the oral gel showed greater accumulation of biofilm and the presence of inflammation.

CHX is considered the gold standard in the antiseptic treatment of the oral mucosa because of its broad antibacterial spectrum [15]. However, studies have shown that CHX has a cytotoxic effect on gingival fibroblasts [16], gingival epithelial cells [17], periodontal ligament cells [18], cultured alveolar bone cells [19] and osteoblastic cells interfering with tissue regeneration processes [20]. Although CHX has proven and effective bactericidal activity, these factors can interfere with the healing process. This way, new product options for biofilm control along with stimulating the healing process, with topical oxygen release (blue®m oral care), are available for use in clinical and surgical procedures, presenting good clinical [21] and scientific results [22, 23]. This can be observed in the healing process of the clinical cases presented here.

Conclusion

As a result of the observation by comparison in both clinical cases, it is suggested that the use of active oxygen in oral gel (blue®m) as an antiseptic and stimulate agent of healing to surgical oral wounds. Is indicate a reliable and safe alternative for the post-surgical care of oral wounds after the placement of dental implants, in these clinical

cases it optimized wound healing. Studies are required to support this suggestion.

Consent

Patient signed written consent regarding publishing her data and photographs.

Conflicts of Interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

REFERENCES

[1] Kadkhodazadeh M, Amid R, Moscowchi A, Lakmazaheri E. Short-term and long-term success and survival rates of implants supporting single-unit and multiunit fixed prostheses: A systematic review and meta-analysis. J Prosthet Dent. 2023 Feb 11: S0022-3913(23)00008-2. doi: 10.1016/j.prosdent.2022.12.012.

[2] Raikar S, Talukdar P, Kumari S, Panda SK, Oommen VM, Prasad A. Factors Affectingthe Survival Rate of Dental Implants: A Retrospactive Study. J. Int Soc Prevent Communit Dent 2017; 7:351-5.

[3] Ngeow WC, Tan CC, Goh YC, Deliberador TM, Cheah CW. A Narrative Review on Means to Promote Oxygenation and Angiogenesis in Oral Wound Healing. Bioengineering (Basel). 2022 Nov 2;9(11):636. doi: 10.3390/bioengineering9110636.

[4] Toma AI, Fuller JM, Willett NJ, Goudy SL. Oral wound healing models and emerging regenerative therapies. Transl Res. 2021 Oct;236:17-34. doi: 10.1016/j.trsl.2021.06.003.

[5] Pulito C, Cristaudo A, Porta C, Zapperi S, Blandino G, Morrone A, Strano S. Oral mucositis: the hidden side of cancer therapy. J Exp Clin Cancer Res. 2020 Oct 7;39(1):210. doi: 10.1186/s13046-020-01715-7.

[6] Sen CK. Wound healing essentials: let there be oxygen. Wound Repair Regen. 2009 Jan-Feb;17(1):1-18. doi: 10.1111/j.1524-475X.2008.00436.x.

[7] Younis I. Role of oxygen in wound healing. J Wound Care. 2020 May 1;29(Sup5b): S4-S10. doi: 10.12968/jowc.2020.29.Sup5b.S4

[8] Deliberador TM, Macalossi JMS, Tenorio C, Dall Agnol GS, Boia MF, Zielak JC. An oxygen-releasing agent promotes healing of skin wounds in rats. J Wound Care. 2023 Nov 2;32(11):738-747. doi: 10.12968/jowc.2023.32.11.738.

[9] Wachtel H, Schenk G, Böhm S, Weng D, Zuhr O, Hürzeler MB. Microsurgical access flap and enamel matrix derivative for the treatment of periodontal intrabony defects: a controlled clinical study. J Clin Periodontol. 2003 Jun;30(6):496-504. doi: 10.1034/j.1600-051x.2003.00013.x

[10] Covani U, Marconcini S, Crespi R, Barone A. Bacterial plaque colonization around dental implant surfaces. Implant Dent. 2006 Sep;15(3):298-304. doi: 10.1097/01.id.0000226823.58425.19.

[11] Gabay E, Levin L, Zuabi O, Horwitz J. Plaque score change as an indicator for periimplant health in periodontal patients with immediately restored dental implants. Implant Dent. 2015 Jun;24(3):323-7. doi: 10.1097/ID.0000000000000236.

[12] Knighton DR, Hunt TK, Scheuenstuhl H, Halliday BJ, Werb Z, Banda MJ. Oxygen tension regulates the expression of angiogenesis factor by macrophages. Science. 1983 Sep 23;221(4617):1283-5. doi: 10.1126/science.6612342.

[13] Eisenbud DE. Oxygen in wound healing: nutrient, antibiotic, signaling molecule, and therapeutic agent. Clin Plast Surg. 2012 Jul;39(3):293-310. doi: 10.1016/j.cps.2012.05.001.

[14] 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 May 31;2021:5535807. doi: 10.1155/2021/5535807.

[15] Van Strydonck DA, Slot DE, Van der Velden U, Van der Weijden F. Effect of a chlorhexidine mouthrinse on plaque, gingival inflammation and staining in gingivitis patients: a systematic review. J Clin Periodontol. 2012 Nov;39(11):1042-55. doi: 10.1111/j.1600-051X.2012.01883.x.

[16] Mariotti AJ, Rumpf DA. Chlorhexidine-induced changes to human gingival fibroblast collagen and non-collagen protein production. J Periodontol. 1999 Dec;70(12):1443-8. doi: 10.1902/jop.1999.70.12.1443.

[17] Babich H, Wurzburger BJ, Rubin YL, Sinensky MC, Blau L. An in vitro study on the cytotoxicity of chlorhexidine digluconate to human gingival cells. Cell Biol Toxicol. 1995 Apr;11(2):79-88. doi: 10.1007/BF00767493.

[18] Chang YC, Huang FM, Tai KW, Chou MY. The effect of sodium hypochlorite and chlorhexidine on cultured human periodontal ligament cells. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001 Oct;92(4):446-50. doi: 10.1067/moe.2001.116812.

[19] Cabral CT, Fernandes MH. In vitro comparison of chlorhexidine and povidone-iodine on the long-term proliferation and functional activity of human alveolar bone cells. Clin Oral Investig. 2007 Jun;11(2):155-64. doi: 10.1007/s00784-006-0094-8.

[20] Giannelli M, Chellini F, Margheri M, Tonelli P, Tani A. Effect of chlorhexidine digluconate on different cell types: a molecular and ultrastructural investigation. Toxicol In Vitro. 2008 Mar;22(2):308-17. doi: 10.1016/j.tiv.2007.09.012

[21] Shaheen MY, Abas I, Basudan AM, Alghamdi HS. Local Oxygen-Based Therapy (blue®m) for Treatment of Peri-Implant Disease: Clinical Case Presentation and Review of Literature about Conventional Local Adjunct Therapies. Medicina (Kaunas). 2024 Mar 8;60(3):447. doi: 10.3390/medicina60030447.

[22] Santos VCED, Maquera-Huacho PM, Imbriani MJM, Minhaco VMTR, Spolidorio DMP. Effects of BlueM® against Streptococcus mutans biofilm and its virulence gene expression. Braz Dent J. 2023 Jan-Feb;34(1):19-28. doi: 10.1590/0103-6440202305133. PMID: 36888841; PMCID: PMC10027103.

[23] Cláudio MM, Garcia VG, Freitas RM, Rodrigues JVS, Wainwright M, Casarin RCV, Duque C, Theodoro LH. Association of active oxygen-releasing gel and photodynamic therapy in the treatment of residual periodontal pockets in type 2 diabetic patients: A randomized controlled clinical study. J Periodontol. 2023 Dec 19. doi: 10.1002/JPER.23-0125.

Figures and Figures Legends

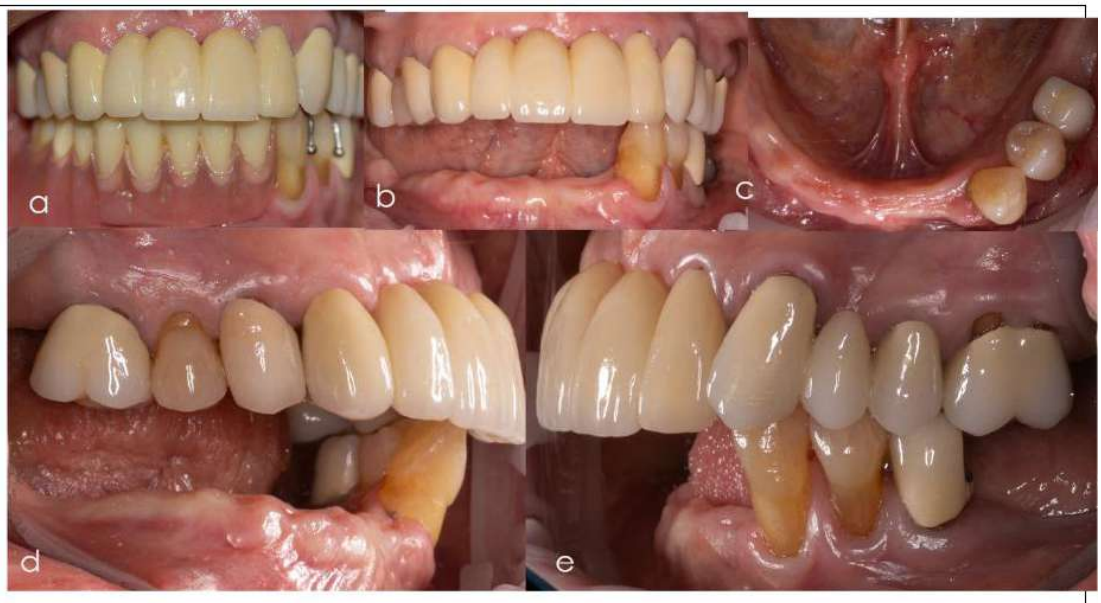

Figure 1: Initial clinical condition of patient one. a) Frontal view with the lower removable prosthesis, b) Frontal view without the lower removable prosthesis, c) Occlusal view of the lower arch, d) right lateral view, e) left lateral view.

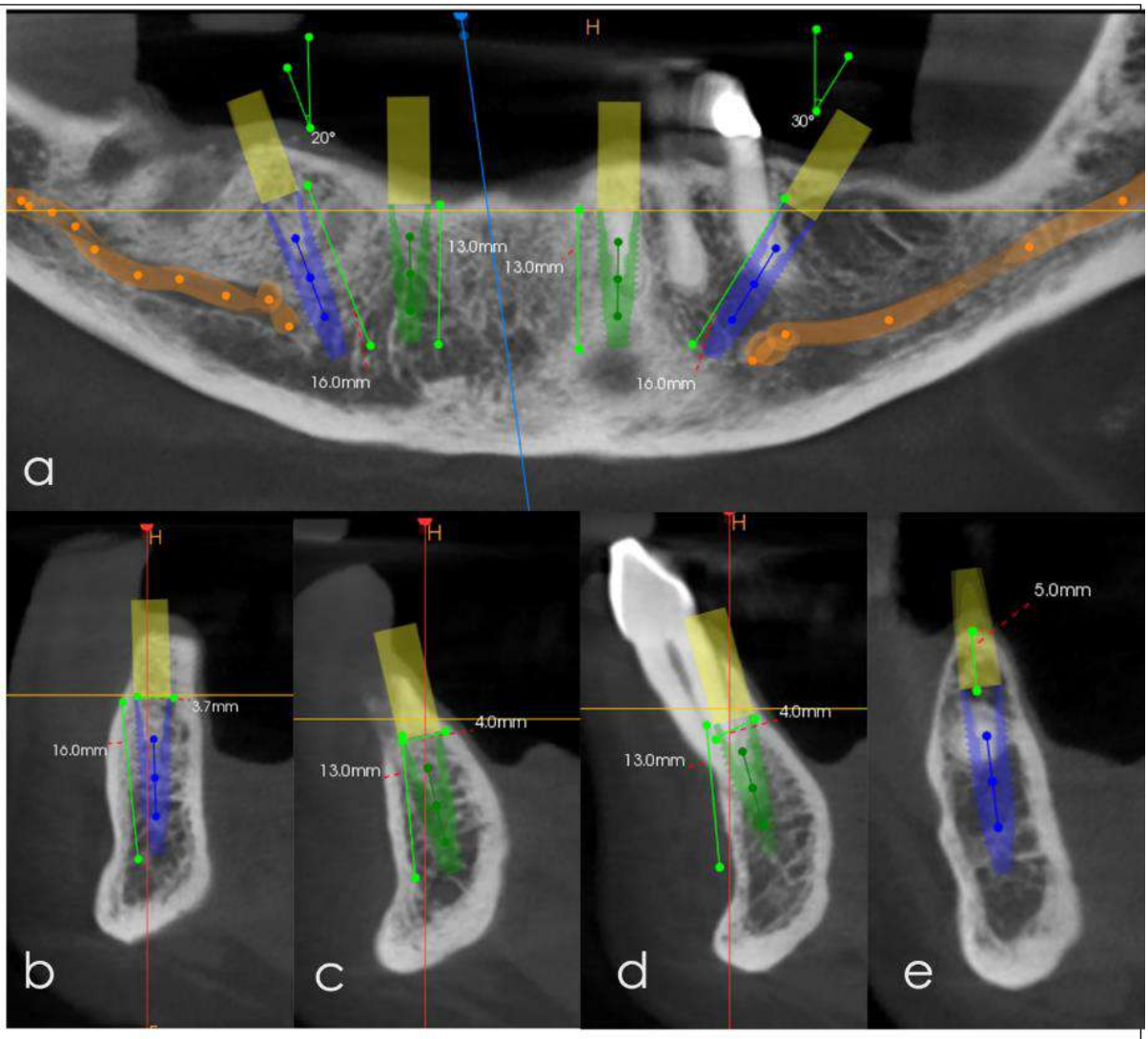

Figure 2: Digital planning of the length and diameter of the implants to be installed in the lower arch in patient one (a-e).

Figure 3: **Initial** clinical condition of patient two. a) Front image, b) right side image, c) left side image.

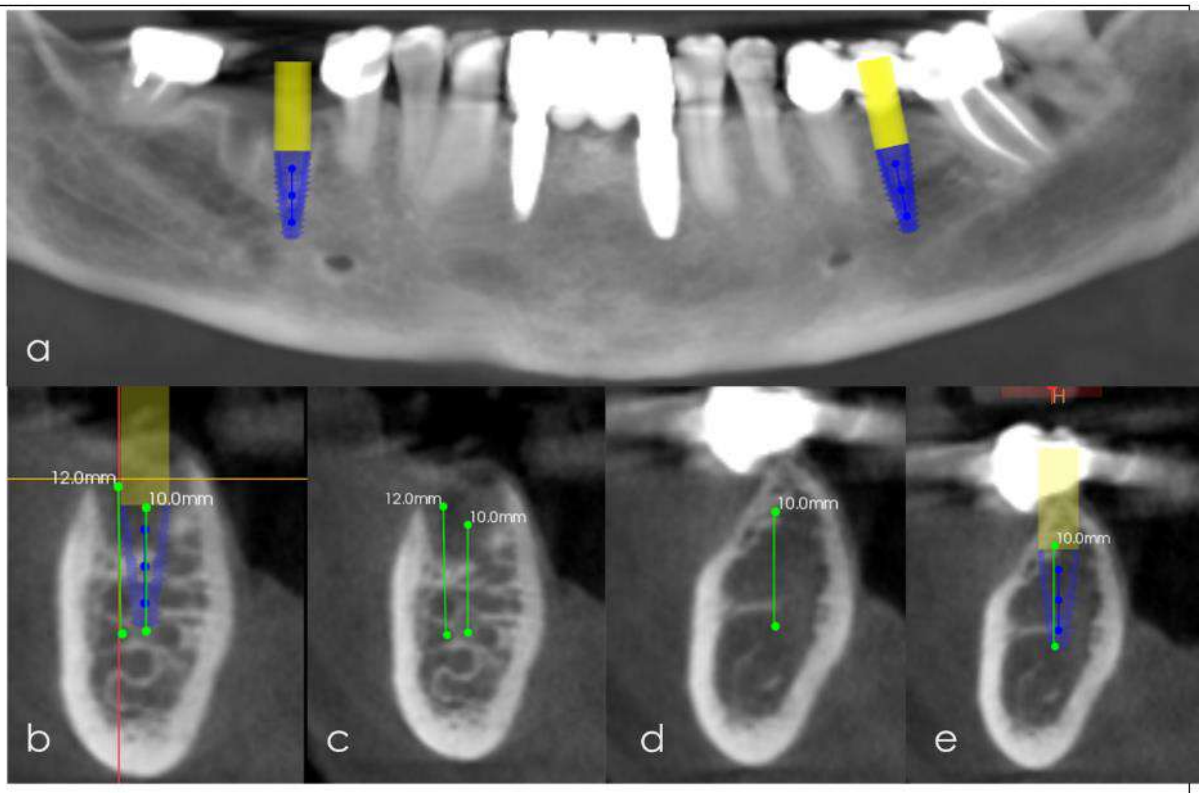

Figure 4: Digital planning of the length and diameter of the implants to be installed in the lower arch in patient two (a-e).

Figure 5: a) Multifunctional guide seating after extraction of remaining teeth and reflection of the full-thickness flap, b) location of the mental foramen with pencil marking to evaluate the relationship between the installation of the distal implant and the required angulation, c) checking parallelism between implants, d) four implants installed in the lower arch.

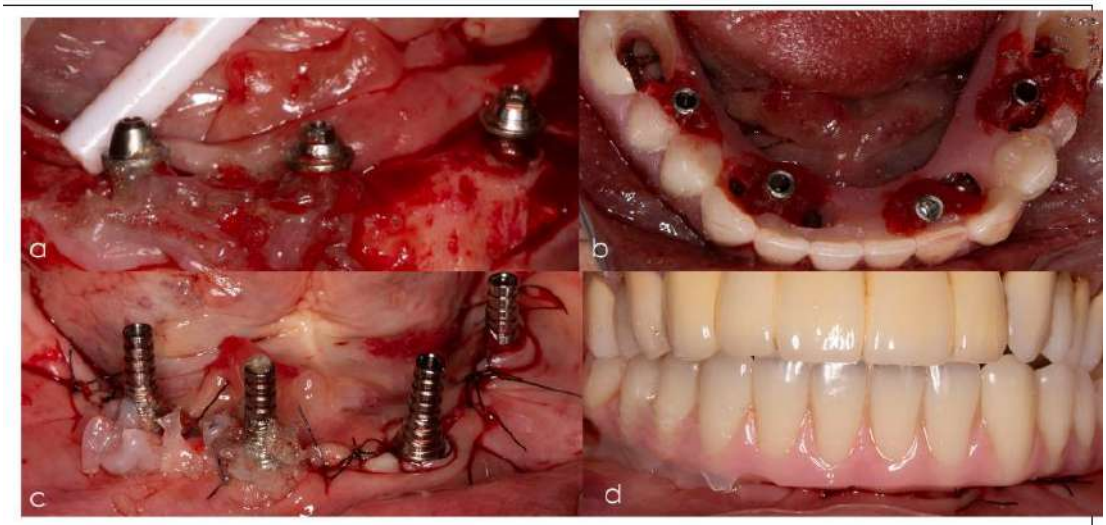

Figure 6: a) Active oxygen gel (blue®m) was placed on the surgical site in the right implants before flap suturing, b) Capture of the provisional complete denture, c) Application of active oxygen gel (blue®m), only in the right side after suturing the flap, installing the impression cylinders and capture of the provisional complete denture, d) Provisional total prosthesis installed over the 4 implants. The patient was recommended to apply the oral gel at home every 8 hours only on the right side.

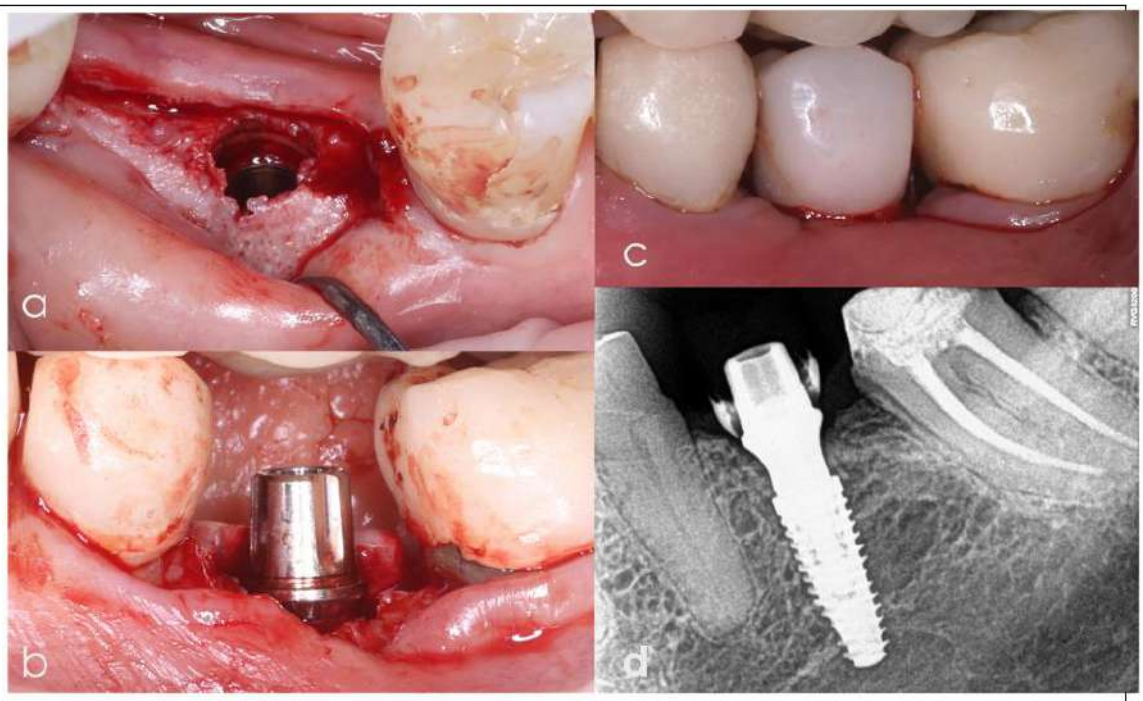

Figure 7: Patient two. Left side a) 2 mm intraosseous implant installed, b) universal click GM exact installed, c) temporary prosthesis installed, d) immediate periapical rx at the end of the procedure.

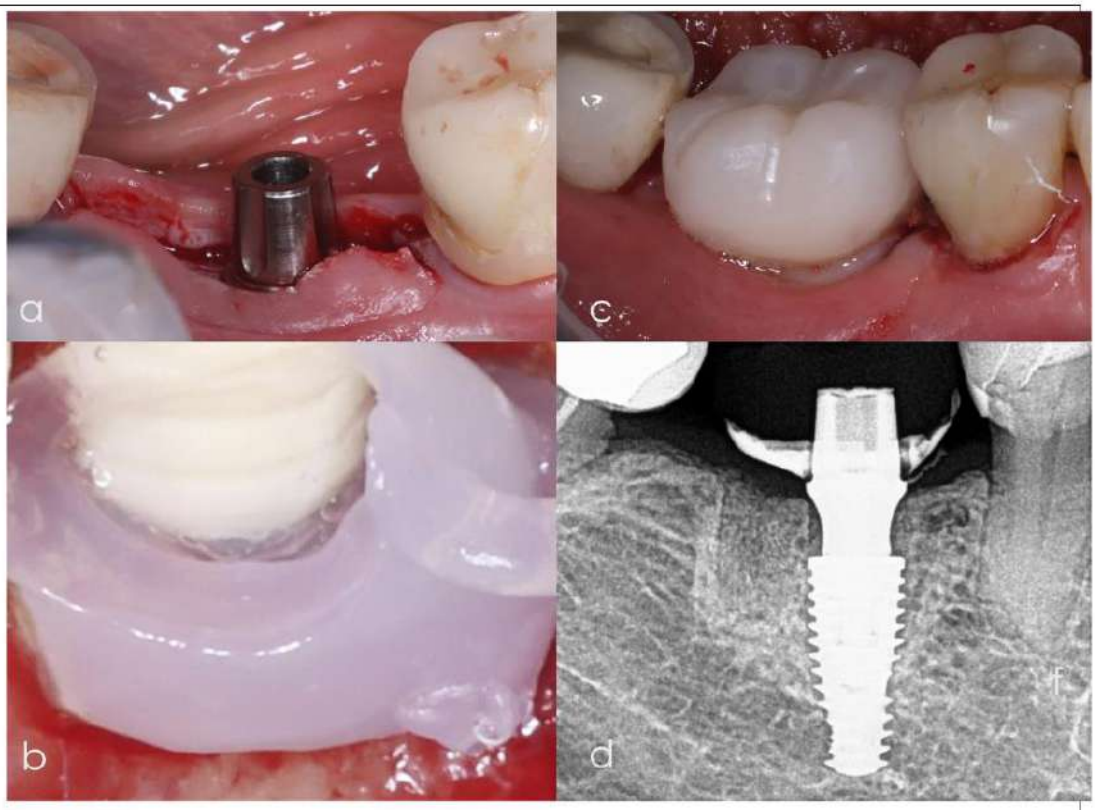

Figure 8: Patient two. Right side a) universal click GM exact installed, b) oral gel with active oxygen applied to the surgical area before closing the flap, c) temporary prosthesis installed, d) immediate periapical rx at the end of the procedure.

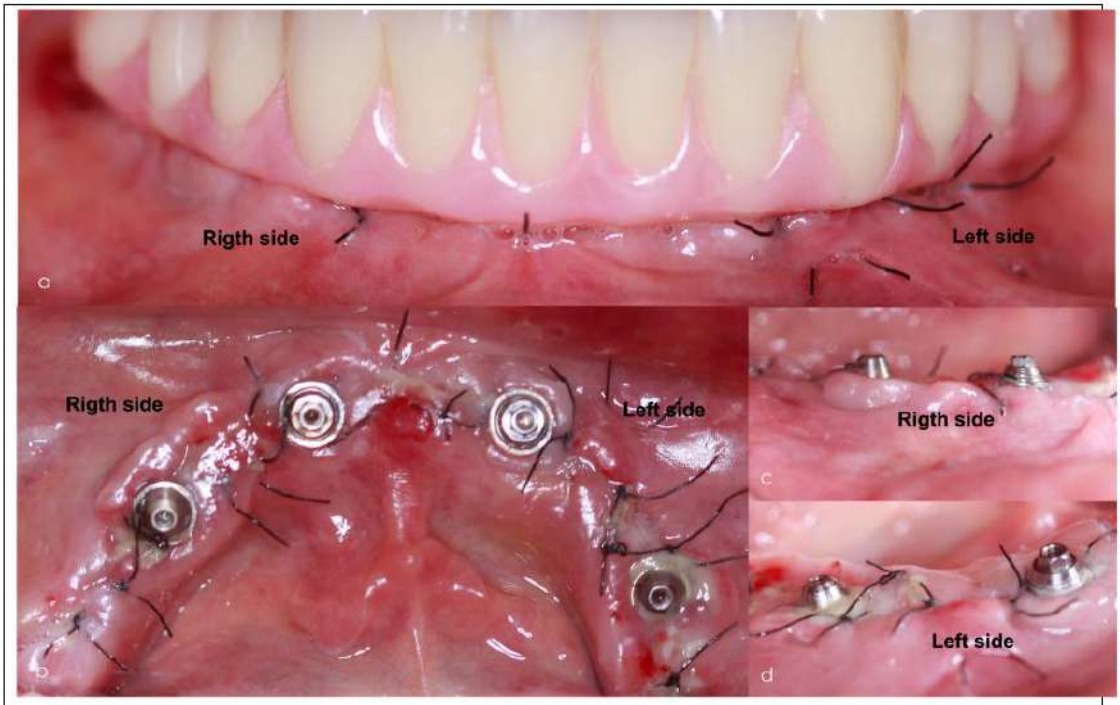

Figure 9: Patient one – 7 days postoperative. a) Image with the temporary prosthesis still in position, b) Occlusal image with the temporary prosthesis removed. It is observed that the right side that received the blue®m oral gel presents better healing, c) Lateral image on the right side, showing total closure of the flap with fine fibrin line in the interproximal area, d) Lateral image on the left side, showing closure of the flap with fibrin clot in the interproximal area.

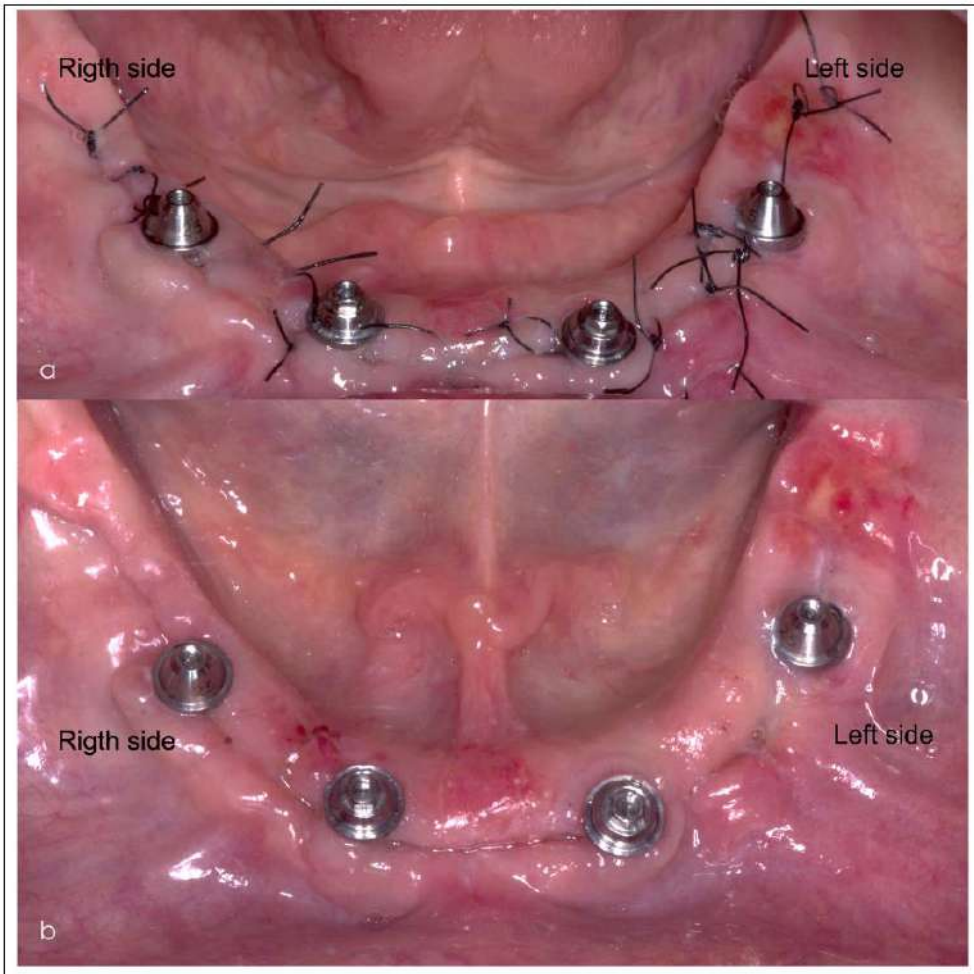

Figure 10: Patient one – 15 days postoperative. a) Image before suture removal shows the right side with better healing than the left side, b) Occlusal image after suture removal, shows the right side with total flap closure without fibrin zones and the left side shows with total flap closure with thin fibrin zones.

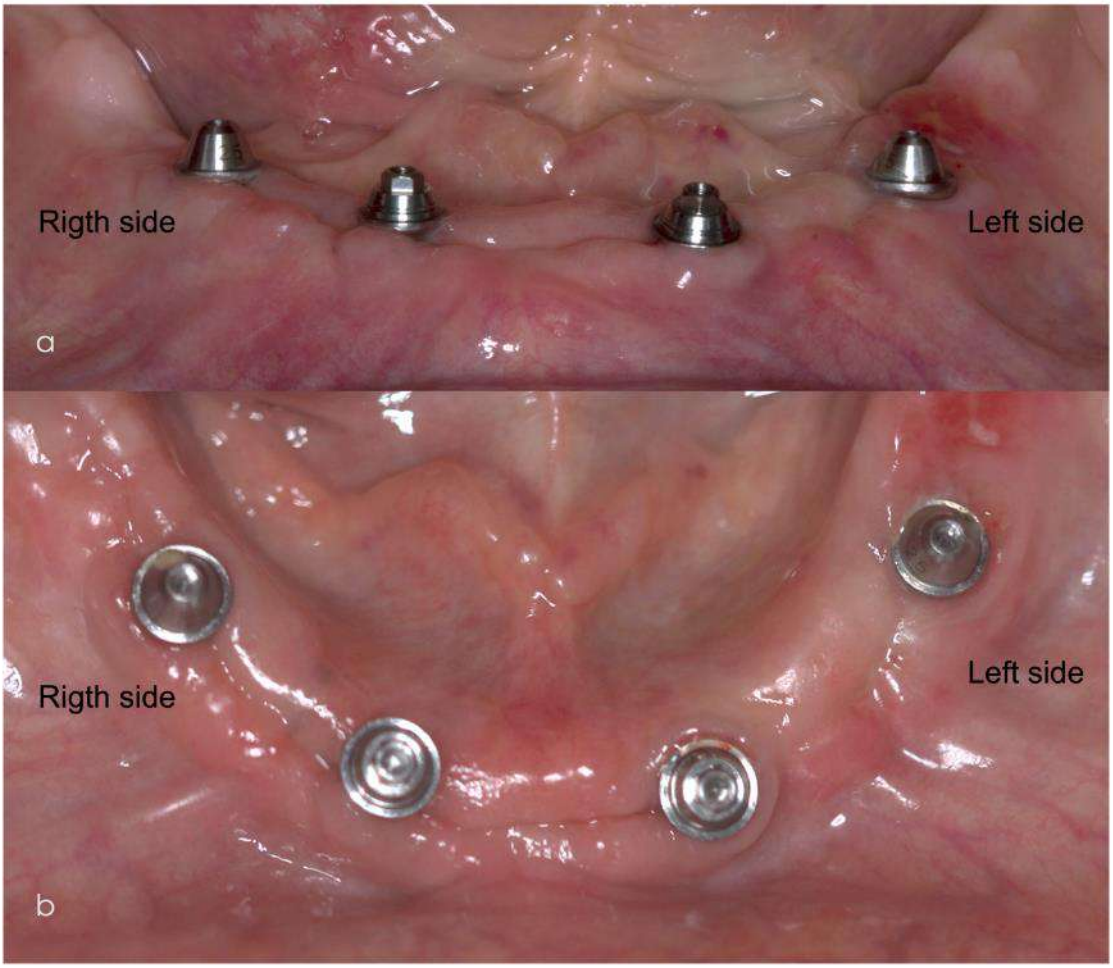

Figure 11: Patient one – 30 days postoperative. a) Frontal Image shows similar healing process between the right and left side b) Occlusal image shows the right side shows with total flap closure without fibrin zones and the left side shows with total flap closure with thin fibrin zones.

Figure 12: Patient two – 3 days postoperative. a) Right side image by buccal, shows complete flap closure with fine fibrin line in the interproximal area, b) Right side image by lingual, shows complete flap closure with fine fibrin line in the interproximal area more evident in the mesial, c) Image on the left side by buccal shows complete flap closure with fine fibrin line in the interproximal area, d) Image on the left side by lingual shows not complete flap closure with fibrin clot in the lingual and interproximal area.

Figure 13: Patient two – 7 days postoperative. a) Right side image by buccal, shows complete flap closure with fine fibrin line in the interproximal area, b) Right side image by lingual, shows complete flap closure with fine fibrin line in the interproximal area more evident in the mesial, c) Image on the left side by buccal shows complete flap closure with fine fibrin line in the interproximal area, d) Image on the left side by lingual shows not complete flap closure with fibrin clot in the lingual and interproximal area.

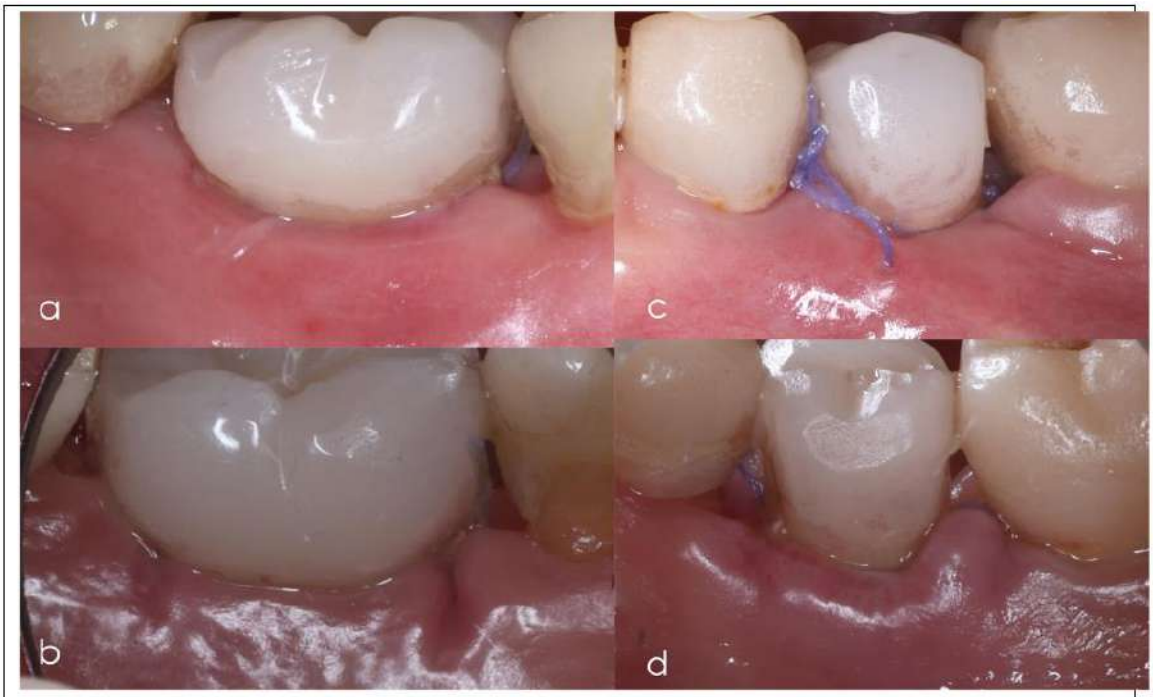

Figure 14: Patient two – 10 days postoperative. a) Right side image by buccal, shows complete flap closure and no fibrin line in the interproximal area and marginal region, b) Right side image by lingual, shows complete flap closure and no fibrin line in the interproximal area and marginal region, c) Image on the left side by buccal shows complete flap closure with fine fibrin line in the interproximal area, d) Image on the left side by lingual shows not complete flap closure fine fibrin line in lingual and the interproximal area.

Figure 15: Patient two – 15 days postoperative. Better healing was observed on the right side a) Right side image by buccal, shows complete flap closure and no fibrin line in the interproximal area and marginal region, b) Right side image by lingual, shows complete flap closure and no fibrin line in the interproximal area and marginal region, c) Image on the left side by buccal shows complete flap closure with fine fibrin line in the interproximal area, d) Image on the left side by lingual shows not complete flap closure fine fibrin line in lingual and the interproximal area.

Figure 16: Patient two – 30 days postoperative. a) Right side image by buccal, shows total flap closure without fibrin, b) Right side image by lingual, shows total flap closure without fibrin, c) Image on the left side by buccal with total closure of the flap and fibrin line marginal to the crown with the presence of inflammation due to bacterial biofilm, d) Image on the left side by lingual shows total closure of the flap and fibrin line marginal to the crown.

Figure 17: Patient two – 60 days postoperative. a) Right side image by buccal, shows complete flap closure and no fibrin line with excellent healing observed in the region, b) Right side image by lingual, shows complete flap closure and no fibrin line, c) Image on the left side by buccal shows complete closure of the flap with incomplete formation of the distal papillae, d) Image on the left side by lingual shows complete closure of the flap and no fibrin line.

Formulário 1
Proposta de Parceria Científica

1. Dados do Demandante

1. Nome:	**BLUEM BRASIL S.A.**
2. CNPJ ou CPF:	26.469.621/0001-02
3. Endereço completo:	Rua México 854, sala 02, Curitiba/PR
4. Pessoa de contato:	Tatiana Deliberador
5. Telefone de contato:	41 999764948
6. E-mail de contato:	academico.cientifico@bluem.com.br

2. Demanda da Empresa

Produto	Gel oral da bluem
Estágio de desenvolvimento	▢ Sem Registro x Pós Venda
Objetivo	Avaliar a cicatrização com uso do gel oral em áreas que receberam implantes dentários
Impacto para a Empresa	( ) Novo processo ( ) Mudança de processo (x) Reforço de marketing ( ) Lançamento de Produto e Educação
Confidencial (restringir disponibilidade na CAPES e site da Ilapeo?)	▢ SIM x NÃO

3. Deliberação (Faculdade Ilapeo)

1. Proposta:	x APROVADA ▢ REJEITADA
2. Responsável pela análise	Ana Claudia Melo

4. Equipe (Faculdade Ilapeo)

1. Professor Coordenador:	Tatiana Miranda Deliberador
2. Equipe Científica do Ilapeo (profissionais):	Tatiana Miranda Deliberador
3. Equipe Científica do Ilapeo (discentes):	Reyna María Ocegueda Estrada

Formulário 3

Relatório Técnico de Projeto Científico

☐PARCIAL / X FINAL

Nº DO PROJETO	CURSO RESPONSÁVEL (MP; DP)
XX/20XX	**MP**

TÍTULO: Use of topical oxygen therapy to optimize postoperative healing of oral surgical wounds after dental implant placement.

ATIVIDADE(S): Relato de caso clínico

PALAVRAS-CHAVE: topical oxygen therapy, oral wound healing, dental implants

RESUMO

Implant-supported and implant-borne prostheses have become a common alternative for treating total or partial edentulous patients with good long-term results. Prompt and effective healing of surgical wounds will contribute to this purpose. The objective of this case report was to evaluate by clinical observation the effect of oral gel with active oxygen (blue®m) on the healing of oral post-surgical wounds following dental implant placement. Two patients underwent dental implant placement surgery by conventional open techniques to evaluate the healing of post-surgical wounds subjected to flaps, both with immediate loading and provisional. In the first one, a full arch surgery with four implants and bone reduction was performed. In the second, two mandibular single implants were placed in sites 46 and 36 with immediate loading and provisional. The active oxygen gel product (blue®m) was placed in the tissues before closing the flap and after suturing. Patients were instructed to place the product only on the right side three times a day and no product or topical medication on the left side. Observational comparisons were made by Early Wound Healing Index (EHI) at 7, 15, and 30-days post-surgery in the complete arch, and 3, 7, 10, 15, 30, and 60-days in the single cases. As a

result of the observation by comparison in both clinical cases, it is suggested that the use of active oxygen in oral gel (blue®m) as an antiseptic and stimulate agent of healing to surgical oral wounds. Is indicate a reliable and safe alternative for the post-surgical care of oral wounds after the placement of dental implants, in these clinical cases it optimized wound healing. Studies are required to support this suggestion.

AUTOR(ES): Reyna María Ocegueda Estrada e Tatiana Miranda Deliberador

TATIANA MIRANDA DELIBERADOR

Responsável Técnico

SUMÁRIO

5. OBJETIVO

The objective of this case report was to evaluate by clinical observation the effect of oral gel with active oxygen (blue®m) on the healing of oral post-surgical wounds following dental implant placement.

6. INTRODUÇÃO

Treatment with Osseo integrated dental implants is a predictable and widespread treatment alternative to omit the need for fixed dentures or removable prostheses in the rehabilitation of edentulous patients with predictable short- and long-term success rates [1]. The factors that determine the success and survival of implants are related to the host, the implant, the prosthesis, and the surgery [2]. In this last point, the healing of the surgical wound will reestablish the protection barrier against pathogenic invaders, mechanical stresses, and physical trauma [3]. Four consecutive

stages of tissue change occur in this healing: hemostasis, inflammation, proliferation, and remodeling. Hemostasis and inflammation will begin from the time of injury and continue for up to four to six days. The proliferation stage means re-epithelialization, angiogenesis, granulation tissue formation, and collagen deposition. This phase starts from day four and will last up to three weeks after a soft tissue injury. The soft and/or hard tissue remodeling phase will continue for approximately one year [4]. Wound healing in the mouth is driven by the inflammatory and vascular response, at this point angiogenesis or neovascularization plays a significant role. Capillary growth is necessary for optimal wound healing by providing oxygen and micronutrients and removing catabolic waste products from the healing tissues [5].

Therapeutic approaches aimed at improving tissue oxygenation may be the key to success in wound management [6]. Oxygen is an essential element for the maintenance of healthy tissues and for wound healing processes [7]. Hypoxia in the wound is natural in tissue injury, it requires energy and balance in oxygen production for neovascularization and epithelialization [3,7]. Hyperbaric oxygen therapy and topical oxygen have been reported to improve wound healing [6]. Other means promote angiogenesis in oral wound healing during the proliferation process, such as ultrasound, lasers, platelet-rich plasma (PRP)/platelet-rich fibrin (PRF), and various chemical agents such as hyaluronic acid, anthoxanthin and Centella asiatica. These include cutting-edge therapies such as the use of growth factors, bioengineered skin substitutes, and stem cell therapy [3].

There is currently a product on the market focused on the principle of improving topical oxygen delivery to wounds oral care (blue®m). This easy-to-use product seems to positively influence tissue healing by improving oxygenation without risking the stability of the microbiome. The slow and continuous release of oxygen in (blue®m) in the tissues arises from the components present in the formula honey (glucose oxidase enzyme) and sodium perborate. When these ingredients meet tissue fluids, they are transformed into hydrogen peroxide (H_2O_2) at low concentrations (0.003 to 0.15%). The oral gel is the product with the highest amount of oxygen release, thus its healing and bactericidal actions [3,8].

7. DESENVOLVIMENTO

Diagnosis and Treatment Plan:

Patient one

A 74-year-old female patient, systemically healthy, came to the clinic with the need to change her lower removable prosthesis for a fixed treatment option to improve her functionality. The upper dental arch had a fixed prosthesis on teeth and the lower arch had a Kennedy class I with only three remaining teeth on the left side (Figure 1).

After a comprehensive clinical and tomographic examination (Figure 2), the treatment plan consisted of performing a full arch protocol on four mandibular implants with provisional and immediate loading, (Neo Arch technique Neodent®) with vertical bone reduction, and conventional open surgical technique to evaluate healing in wide wounds. The oral gel with active oxygen release (blue®m) was placed on the implants and right surgical site before and after flap closure and the patient placed the gel three times a day only on the right side during the evolution of the wound (clinical observation were made at 7, 15, and 30-days post-surgery) to compare the healing with the left side where no topical product or medication was indicated.

8. **Patient two.**

A systemically healthy 67-year-old female patient came for a consultation to have fixed prosthetic teeth in edentulous sites 46 and 36 after her diagnostic examination and evaluation of her initial situation (Figure 3). After a comprehensive clinical and tomographic examination (Figure 4), the treatment plan consisted of placing two osseointegrated dental implants in these sites with provisional and immediate loading. Placed with conventional freehand surgery to evaluate the healing after wounds with flaps.

The active oxygen extended-release gel (blue®m) was placed on the implant and right surgical site before and after flap closure and the patient placed the gel topically three times a day only on the right side during the evolution of the wound (clinical observation were made at 3, 7, 10, 15, 30 and 60-days post-surgery) to compare the healing with the left side where no topical product or medication was indicated.

Surgical procedure:

All surgical procedures were performed by the same operator.

Patient one

The surgical procedure was started with asepsis and antisepsis, and local anesthesia was administered right and left mandibular regional block with mepivacaine-epinephrine 36 mg/ 0.018 mg

1.8 ml (Scandonest 2% Special France Septodont.). Exodontia was performed on teeth 33, 34, and 35. An incision was made along the entire alveolar ridge in an extension equivalent to the site from the right first molar to the left first molar with two posterior vestibular discharges using a scalpel blade 15c.

A full-thickness flap was displaced confirming the seating of the multifunctional guide (Figure 5a). The predetermined osteotomy was performed with surgical gouges and drills and the emergence of the right and left mental nerves was visually located and marked with sterile graphite (Figure 5b). The complete drilling sequence for the posterior implants was performed, the emergences were designed at the level of the second premolars, and the posterior implants were placed with an inclination of approximately 17 degrees (Figure 5 c-d).

The implants were installed according to the manufacturer's recommendations (HELIX GM ACQUA, Neodent®, Curitiba/PR, Brazil). All implants achieved torque of more than 32 Ncm. The trans-mucosal prosthetic attachments were then placed as follows. A conical angulated conical minipilar GM exact 17 degrees Neodent® on the right and left posterior implants with a torque of 20 Ncm. A minipilar conical GM Neodent® on the right and left anterior implants with a torque of 32 Ncm.

Active oxygen gel (blue®m) was placed on the surgical site in the right implants (Figure 6a), and the wound synthesis was performed, eight single stitches were made until total closure was achieved using 4-0 nylon. The maneuvers for the capture and adjustment of the provisional denture were immediately performed on four temporary titanium cylinders for the GM mini conical abutment (Figure 6b). Before placing the provisional prosthesis already adjusted and polished, active oxygen gel (blue®m) was placed again on the wound already sutured on the right side (Figure 6c).

The patient was prescribed the antibiotic amoxicillin/clavulanic acid 875/125 mg every 12 hours for 7 days and ibuprofen 400 mg every 8 hours for 3 days.

As part of the post-surgical instructions, the patient was instructed to apply active oxygen gel (blue®m) three times a day only on the wound on the right side, applying it on the vestibular and lingual side until it was placed on the right wound every day until the end of the wound healing follow-up (Figure 6d).

9. **Patient two**

The surgical procedure was started with asepsis and antisepsis, and local anesthesia was administered right and left mandibular regional block with mepivacaine-epinephrine 36 mg/ 0.018 mg

1.8 ml (Scandonest 2% Special France Septodont). Surgery on the right and left sides were performed on the same day by the same operator.

In the left side an incision was made through the alveolar ridge corresponding to site 36, now edentulous and sulcular to the proximal face of the neighboring teeth. A full-thickness flap was reflected, and a drilling sequence was performed up to drill 3.5. It was an area with the medullary bone of low density, a HELIX GM ACQUA 3.75x10 mm (Neodent®, Curitiba/PR, Brazil) implant was placed, as well as an intraosseous placement of 2mm to the vestibular crest (Figure 7a) with a torque of 32 Ncm. A universal click GM exact 4.5x4x3.5 universal stem (Neodent®, Curitiba/PR, Brazil) was installed with a torque of 20 Ncm (Figure 7b). The wound was sutured with stitches at the level of the proximal papillae with polyglactin 910 4-0, and a temporary prosthesis was placed (Figure 7c) in sub occlusion without cement using the temporary click cylinder of the GM universal stump system. Immediate periapical x-ray was performed to verify the correct position of the implant and adaptation of the prosthetic component (Figure 7d).

In the right side an incision was made along the entire alveolar ridge corresponding to site 46, now edentulous and sulcular to the proximal face of the neighboring teeth. A full-thickness flap was reflected, and a complete drilling sequence was performed, a HELIX GM ACQUA 4.3x10 mm (Neodent®, Curitiba/PR, Brazil) implant was placed. Intraosseous placement 2.5mm to the vestibular ridge with a torque of 32 Ncm. A universal click GM exact 4.5x4x3.5 universal stem with 20 Ncm torque was installed (Neodent®, Curitiba/PR, Brazil) (Figure 8a), after was apllied active oxygen gel (blue®m) was then placed in the surgical area (Figure 8b). The wound was sutured with stitches at the level of the proximal papillae with polyglactin 910 4-0, and a temporary prosthesis was placed in sub occlusion (Figure 8c) Immediate periapical x-ray was performed to verify the correct position of the implant and adaptation of the prosthetic component (Figure 8d). At the end of the surgery, the oral gel with active oxygen was applied again.

The patient was prescribed oral antibiotic amoxicillin 500 mg every 8 hours for 7 days and ibuprofen 400 mg every 8 hours for 3 days. As post-surgical indications, the patient was asked to apply active oxygen gel (blue®m) three times a day (8/8hours) only on the wound on the right side, applying it on the vestibular and lingual side every day until the end of the healing follow-up.

Monitoring of healing, observation, and recording of data using the Early Wound Healing Index (EHI) [9]:

Postoperative healing was assessed by an EHI differentiating between 5 different degrees as described below.

1: complete flap closure – no fibrin line in the interproximal area

2: complete flap closure – fine fibrin line in the interproximal area

3: complete flap closure – fibrin clot in the interproximal area

4: incomplete flap closure – partial necrosis of the interproximal tissue

5: incomplete flap closure – complete necrosis of the interproximal tissue

Patient one

Clinical observational with EHI was made at 7, 15, and 30-days post-surgery both on the right and left side (Table 1). The patient received the oral gel with active oxygen only on the right side of surgery.

On postoperative day seven (Figure 9), on the right side, an Index 2 (EHI) with total closure of the flap and the presence fine fibrin line in the interproximal area (Figure 9b-c). On the left side, an Index 3 (EHI) was determined with total closure of the flap with the presence of more fibrin clots along the wound and bleeding points (Figure 9b-d).

On the fifteenth day after surgery the right side shows with better healing than the left side (Figure 10a-b). The right side shows an Index 1 (EHI) total flap closure without fibrin zones (Figure 10b) and the left side shows an Index 2 (EHI) total flap closure with thin fibrin zones (Figure 10b).

On the thirtieth postoperative day, shows similar healing process between the right and left side. However, the right side where the oral gel was applied shows a smaller healing line (Figure 11a-b). The right side shows an Index 1 (EHI) with total flap closure without fibrin areas (Figure 11b), and the left side shows an Index 2 (EHI) with total flap closure, fine fibrin lines in the posterior area of the wound, and still noticeable wound edges. (Figure 11b).

Patient two

Clinical observational with EHI was made at 3, 7, 10, 15, 30, and 60-days post-surgery both on the right (buccal and lingual) and left side (buccal and lingual) (Table 2). The patient received the oral gel with active oxygen only on the right side of surgery.

On day three post-surgery, on the right side an Index 2 (EHI) was observed on the vestibular (Figure 12a) and lingual (Figure 12b) side with total flap closure and a fibrin line in the interproximal

region. On the left side an Index 2 (EHI) was observed on the vestibular side with total flap closure and a cervical fibrin line (Figure 12c) and on the lingual side an Index 3 (EHI) was observed with not total flap closure and wide fibrin clots marginal to the crown (Figure 12d).

On day seven post-surgery, on the right side (Figure 13a-b), an Index 1 (EHI) was observed on the vestibular side with total closure of the flap and no fibrin line in the interproximal area and marginal region (Figure 13a), and on the lingual side an Index 2 (EHI) was observed with total closure of the flap and a fine fibrin line in the marginal region (Figure 13b). On the left side (Figure 13c-d), an Index 2 (EHI) was observed on the vestibular side with total flap closure and a cervical and interproximal fibrin line (Figure 13c), and on the lingual side an Index 3 (EHI) was observed with total flap closure and wide fibrin clots marginal to the crown and interproximal region (Figure 13d). It is clear from clinical observation that the right side showed better healing than the left side.

On postoperative day ten, on the right side (Figure 14a-b), an Index 1 (EHI) was observed on the vestibular and lingual side with total flap closure and no fibrin line in the interproximal area and marginal region. On the left side (Figure 14c-d) an Index 2 (EHI) was observed on the vestibular and lingual side with total flap closure and a cervical fibrin line. Through clinical observation, it is clear, mainly on the lingual side, that the right side showed better healing.

On postoperative day fifteen, better healing was observed on the right side where the oral gel with active oxygen was used. On the right side (Figure 15a-b), an Index 1 (EHI) was observed on the vestibular and lingual side with total flap closure without fibrin. On the left side (Figure 15c-d), an Index 2 (EHI) was observed on the vestibular and lingual side with total flap closure and an interproximal fibrin line.

On postoperative day thirty, on the right side (Figure 16a-b), an Index 1 (EHI) was observed on the vestibular and lingual side with total flap closure without fibrin. On the left side (Figure 16c-d), an Index 2 (EHI) was observed on the vestibular and lingual side with total closure of the flap and fibrin line marginal to the crown. The presence of inflammation was observed due to bacterial biofilm in vestibular side.

On day sixty post-surgery, on the right side (Figure 17a-b), an Index 1 (EHI) is observed on the vestibular and lingual side with total flap closure without fibrin. Excellent healing is observed in the region of the cervical margin and the region of the mesial and distal papillae. On the left side (Figure 17c-d), an Index 2 (EHI) was observed on the vestibular side. It was observed complete closure of the

flap with incomplete formation of the distal papillae (Figure 17c), and on the lingual side, an Index 1 (EHI) was observed with complete closure of the flap (Figure 17d).

At all post-operative times, the right side showed a better healing process compared to the left side where the oral gel with active oxygen release was not applied.

Table 1. Clinical observational with EHI in 7, 15, 30-days post-surgery on right and left side in the patient one.

Postoperative Day.	EHI Right side	EHI Left Side
7 days	2	3
15 days	1	2
30 days	1	2

Table 2. Clinical observational with EHI in 3, 7, 15, 30 and 60-days post-surgery on right and left side in the patient two.

Postoperative Day.	EHI Right Buccal Side	EHI Right Lingual Side	EHI Left Buccal Side	EHI Left Lingual Side
3 days	2	2	2	3
7 days	1	2	2	3
10 days	1	1	2	2
15 days	1	1	2	2
30 days	1	1	2	2
60 days	1	1	2	1

10. CONCLUSÃO

11. As a result of the observation by comparison in both clinical cases, it is suggested that the use of active oxygen in oral gel (blue®m) as an antiseptic and stimulate agent of healing to surgical oral wounds. Is indicate a reliable and safe alternative for the post-surgical care of oral wounds after the placement of dental implants, in these clinical cases it optimized wound healing. Studies are required to support this suggestion.

12. REFERÊNCIAS

[1] Kadkhodazadeh M, Amid R, Moscowchi A, Lakmazaheri E. Short-term and long-term success and survival rates of implants supporting single-unit and multiunit fixed prostheses: A systematic review and meta-analysis. J Prosthet Dent. 2023 Feb 11:S0022-3913(23)00008-2. doi: 10.1016/j.prosdent.2022.12.012.

[2] Raikar S, Talukdar P, Kumari S, Panda SK, Oommen VM, Prasad A. Factors Affectingthe Survival Rate of Dental Implants: A Retrospactive Study. J. Int Soc Prevent Communit Dent 2017; 7:351-5.

[3] Ngeow WC, Tan CC, Goh YC, Deliberador TM, Cheah CW. A Narrative Review on Means to Promote Oxygenation and Angiogenesis in Oral Wound Healing. Bioengineering (Basel). 2022 Nov 2;9(11):636. doi: 10.3390/bioengineering9110636.

[4] Toma AI, Fuller JM, Willett NJ, Goudy SL. Oral wound healing models and emerging regenerative therapies. Transl Res. 2021 Oct;236:17-34. doi: 10.1016/j.trsl.2021.06.003.

[5] Pulito C, Cristaudo A, Porta C, Zapperi S, Blandino G, Morrone A, Strano S. Oral mucositis: the hidden side of cancer therapy. J Exp Clin Cancer Res. 2020 Oct 7;39(1):210. doi: 10.1186/s13046-020-01715-7.

[6] Sen CK. Wound healing essentials: let there be oxygen. Wound Repair Regen. 2009 Jan-Feb;17(1):1-18. doi: 10.1111/j.1524-475X.2008.00436.x.

[7] Younis I. Role of oxygen in wound healing. J Wound Care. 2020 May 1;29(Sup5b):S4-S10. doi: 10.12968/jowc.2020.29.Sup5b.S4

[8] Deliberador TM, Macalossi JMS, Tenorio C, Dall Agnol GS, Boia MF, Zielak JC. An oxygen-releasing agent promotes healing of skin wounds in rats. J Wound Care. 2023 Nov 2;32(11):738-747. doi: 10.12968/jowc.2023.32.11.738.

[9] Wachtel H, Schenk G, Böhm S, Weng D, Zuhr O, Hürzeler MB. Microsurgical access flap and enamel matrix derivative for the treatment of periodontal intrabony defects: a controlled clinical study. J Clin Periodontol. 2003 Jun;30(6):496-504. doi: 10.1034/j.1600-051x.2003.00013.x

[10] Covani U, Marconcini S, Crespi R, Barone A. Bacterial plaque colonization around dental implant surfaces. Implant Dent. 2006 Sep;15(3):298-304. doi: 10.1097/01.id.0000226823.58425.19.

[11] Gabay E, Levin L, Zuabi O, Horwitz J. Plaque score change as an indicator for periimplant health in periodontal patients with immediately restored dental implants. Implant Dent. 2015 Jun;24(3):323-7. doi: 10.1097/ID.0000000000000236.

[12] Knighton DR, Hunt TK, Scheuenstuhl H, Halliday BJ, Werb Z, Banda MJ. Oxygen tension regulates the expression of angiogenesis factor by macrophages. Science. 1983 Sep 23;221(4617):1283-5. doi: 10.1126/science.6612342.

[13] Eisenbud DE. Oxygen in wound healing: nutrient, antibiotic, signaling molecule, and therapeutic agent. Clin Plast Surg. 2012 Jul;39(3):293-310. doi: 10.1016/j.cps.2012.05.001.

[14] 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 May 31;2021:5535807. doi: 10.1155/2021/5535807.

[15] Van Strydonck DA, Slot DE, Van der Velden U, Van der Weijden F. Effect of a chlorhexidine mouthrinse on plaque, gingival inflammation and staining in gingivitis patients: a systematic review. J Clin Periodontol. 2012 Nov;39(11):1042-55. doi: 10.1111/j.1600-051X.2012.01883.x.

[16] Mariotti AJ, Rumpf DA. Chlorhexidine-induced changes to human gingival fibroblast collagen and non-collagen protein production. J Periodontol. 1999 Dec;70(12):1443-8. doi: 10.1902/jop.1999.70.12.1443.

[17] Babich H, Wurzburger BJ, Rubin YL, Sinensky MC, Blau L. An in vitro study on the cytotoxicity of chlorhexidine digluconate to human gingival cells. Cell Biol Toxicol. 1995 Apr;11(2):79-88. doi: 10.1007/BF00767493.

[18] Chang YC, Huang FM, Tai KW, Chou MY. The effect of sodium hypochlorite and chlorhexidine on cultured human periodontal ligament cells. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001 Oct;92(4):446-50. doi: 10.1067/moe.2001.116812.

[19] Cabral CT, Fernandes MH. In vitro comparison of chlorhexidine and povidone-iodine on the long-term proliferation and functional activity of human alveolar bone cells. Clin Oral Investig. 2007 Jun;11(2):155-64. doi: 10.1007/s00784-006-0094-8.

[20] Giannelli M, Chellini F, Margheri M, Tonelli P, Tani A. Effect of chlorhexidine digluconate on different cell types: a molecular and ultrastructural investigation. Toxicol In Vitro. 2008 Mar;22(2):308-17. doi: 10.1016/j.tiv.2007.09.012

[21] Shaheen MY, Abas I, Basudan AM, Alghamdi HS. Local Oxygen-Based Therapy (blue®m) for Treatment of Peri-Implant Disease: Clinical Case Presentation and Review of Literature about Conventional Local Adjunct Therapies. Medicina (Kaunas). 2024 Mar 8;60(3):447. doi: 10.3390/medicina60030447.

[22] Santos VCED, Maquera-Huacho PM, Imbriani MJM, Minhaco VMTR, Spolidorio DMP. Effects of BlueM® against Streptococcus mutans biofilm and its virulence gene expression. Braz Dent J. 2023 Jan-Feb;34(1):19-28. doi: 10.1590/0103-6440202305133. PMID: 36888841; PMCID: PMC10027103.

[23] Cláudio MM, Garcia VG, Freitas RM, Rodrigues JVS, Wainwright M, Casarin RCV, Duque C, Theodoro LH. Association of active oxygen-releasing gel and photodynamic therapy in the treatment of residual periodontal pockets in type 2 diabetic patients: A randomized controlled clinical study. J Periodontol. 2023 Dec 19. doi: 10.1002/JPER.23-0125.

ANEXO A

13. ANEXO A – FIGURAS E LEGENDA DAS FIGURAS

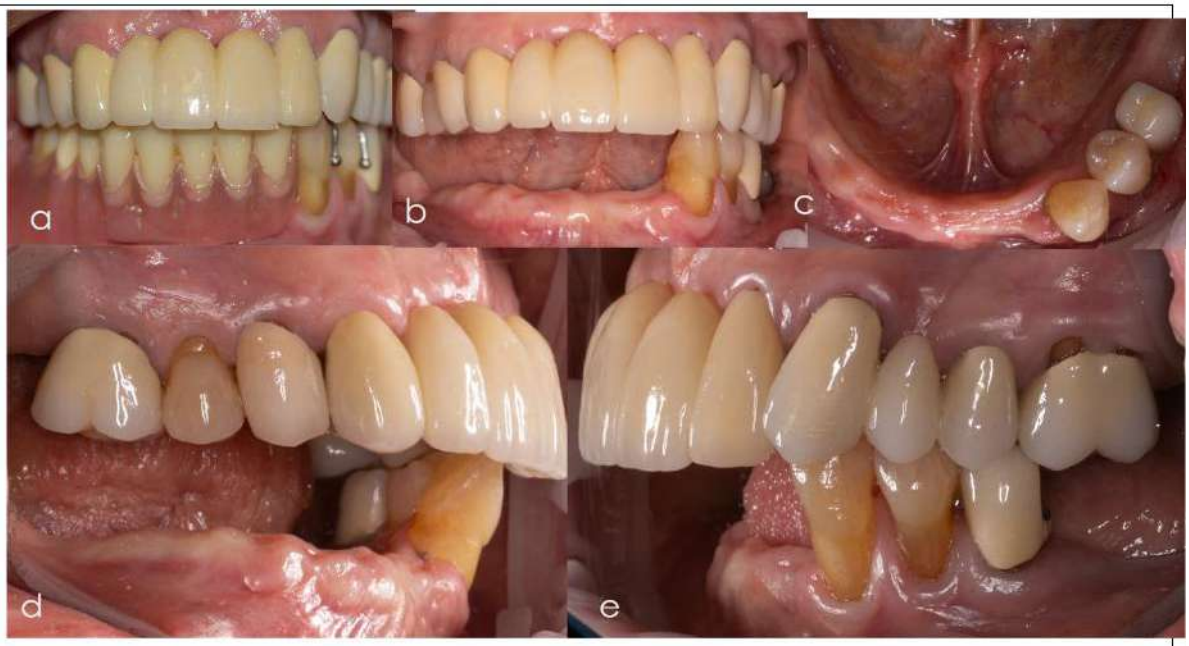

Figure 1: Initial clinical condition of patient one. a) Frontal view with the lower removable prosthesis, b) Frontal view without the lower removable prosthesis, c) Occlusal view of the lower arch, d) right lateral view, e) left lateral view.

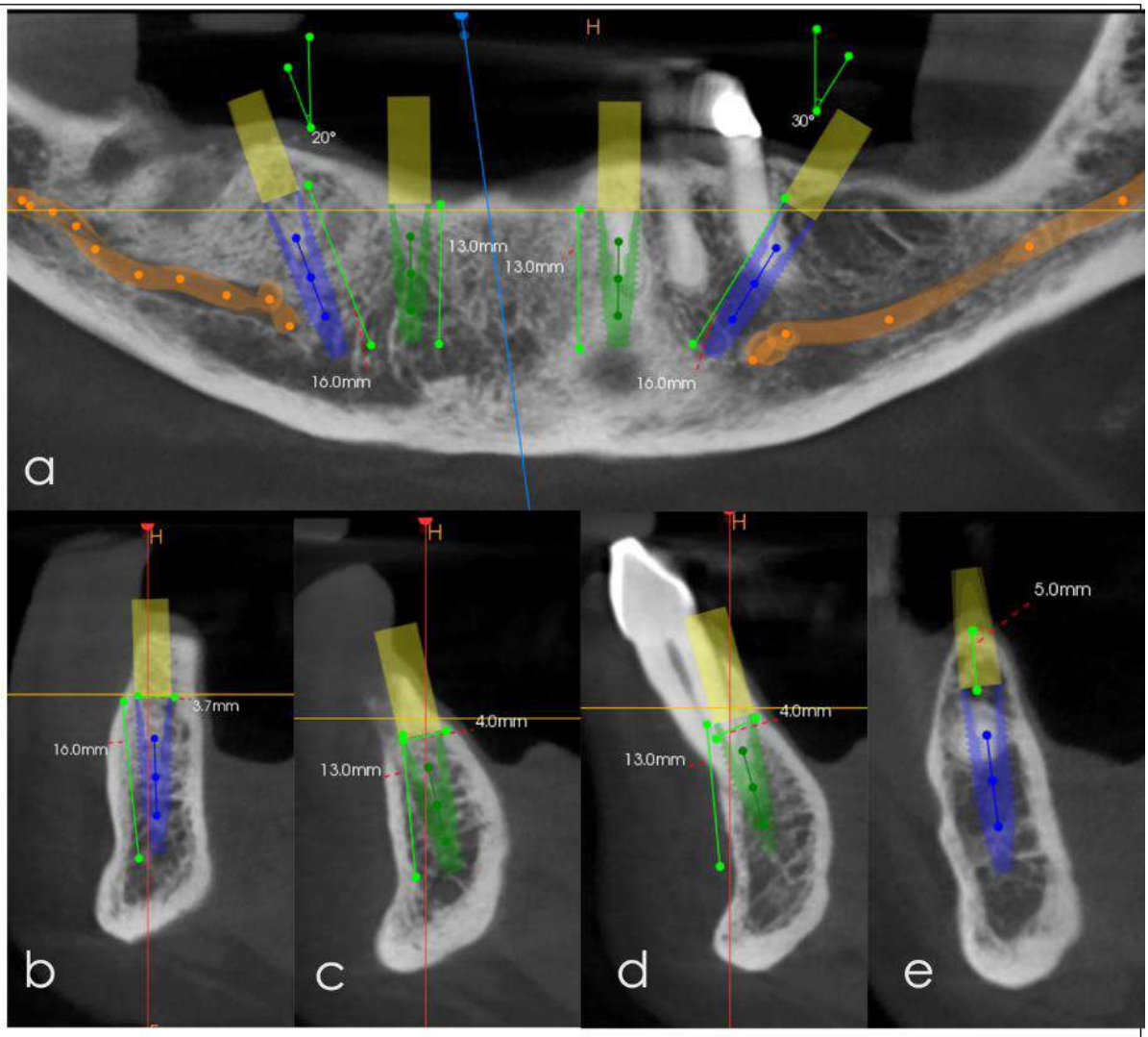

Figure 2: Digital planning of the length and diameter of the implants to be installed in the lower arch in patient one (a-e).

Figure 3: **Initial** clinical condition of patient two. a) Front image, b) right side image, c) left side image.

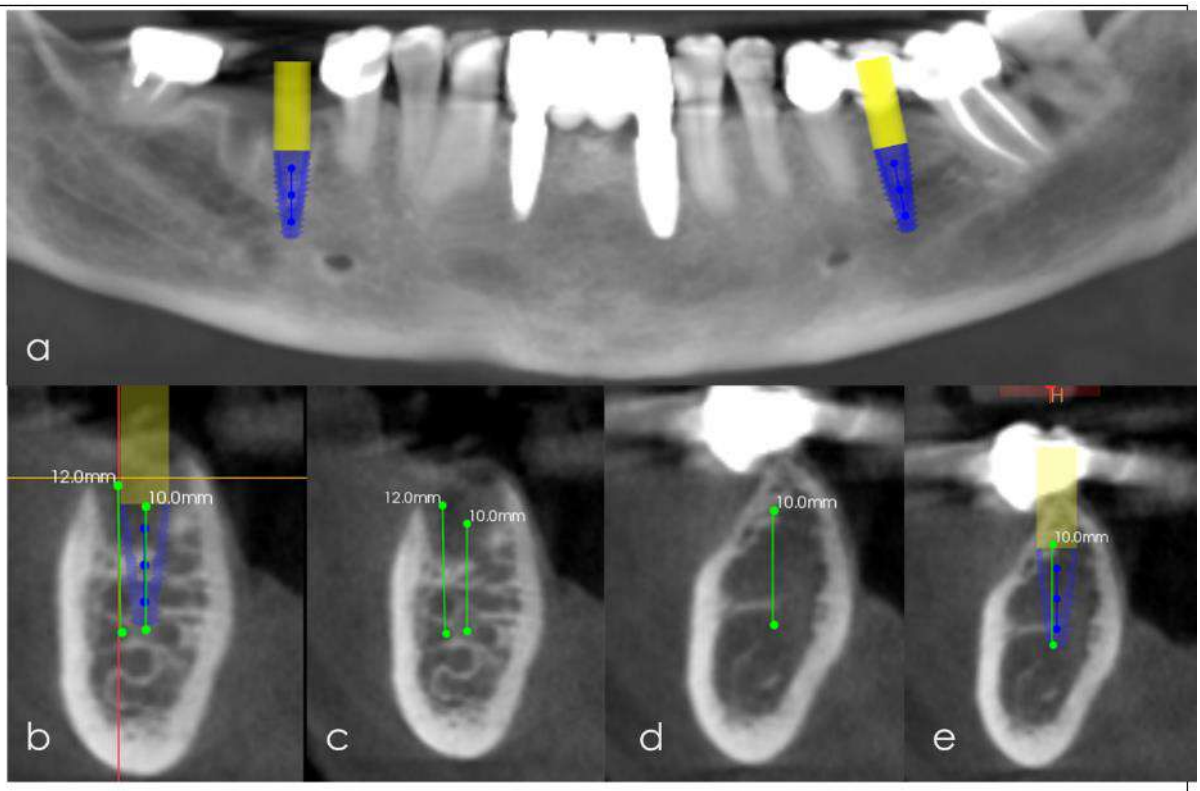

Figure 4: Digital planning of the length and diameter of the implants to be installed in the lower arch in patient two (a-e).

Figure 5: a) Multifunctional guide seating after extraction of remaining teeth and reflection of the full-thickness flap, b) location of the mental foramen with pencil marking to evaluate the relationship between the installation of the distal implant and the required angulation, c) checking parallelism between implants, d) four implants installed in the lower arch.

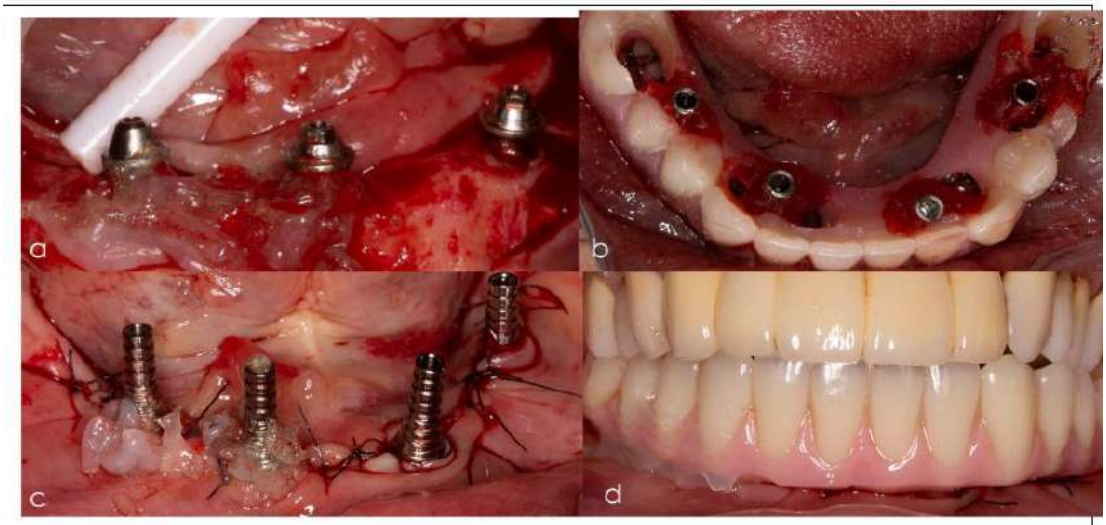

Figure 6: a) Active oxygen gel (blue®m) was placed on the surgical site in the right implants before flap suturing, b) Capture of the provisional complete denture, c) Application of active oxygen gel (blue®m), only in the right side after suturing the flap, installing the impression cylinders and capture of the provisional complete denture, d) Provisional total prosthesis installed over the 4 implants. The patient was recommended to apply the oral gel at home every 8 hours only on the right side.

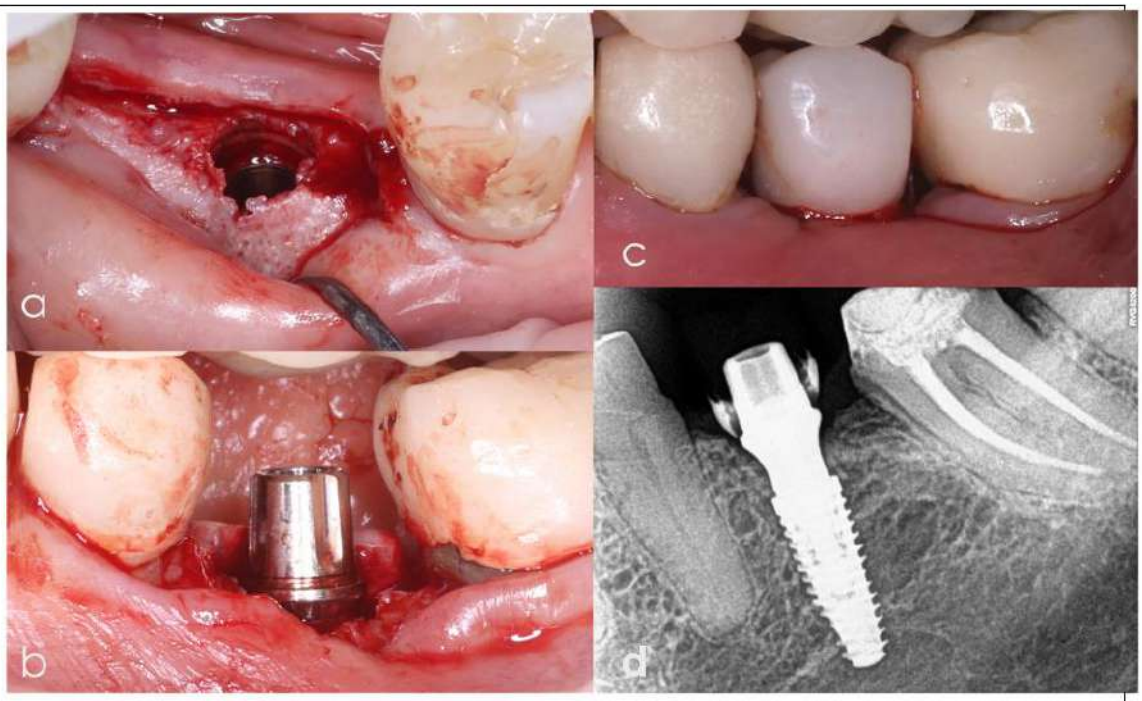

Figure 7: Patient two. Left side a) 2 mm intraosseous implant installed, b) universal click GM exact installed, c) temporary prosthesis installed, d) immediate periapical rx at the end of the procedure.

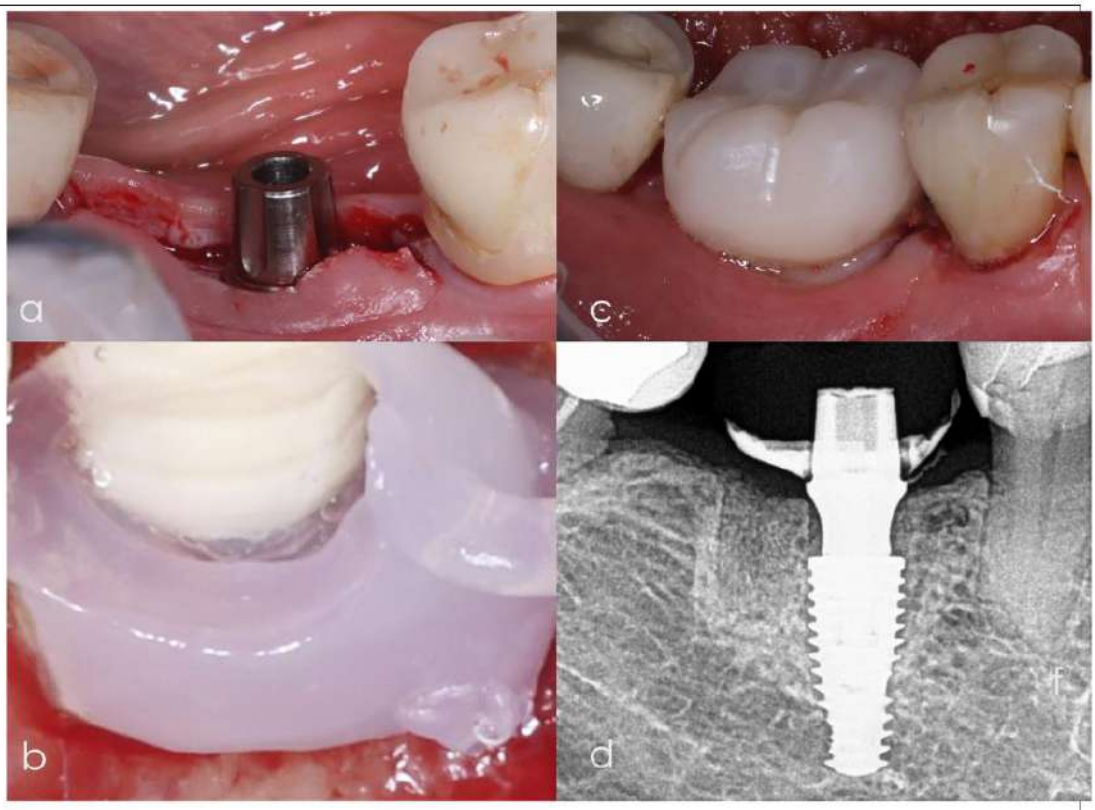

Figure 8: Patient two. Right side a) universal click GM exact installed, b) oral gel with active oxygen applied to the surgical area before closing the flap, c) temporary prosthesis installed, d) immediate periapical rx at the end of the procedure.

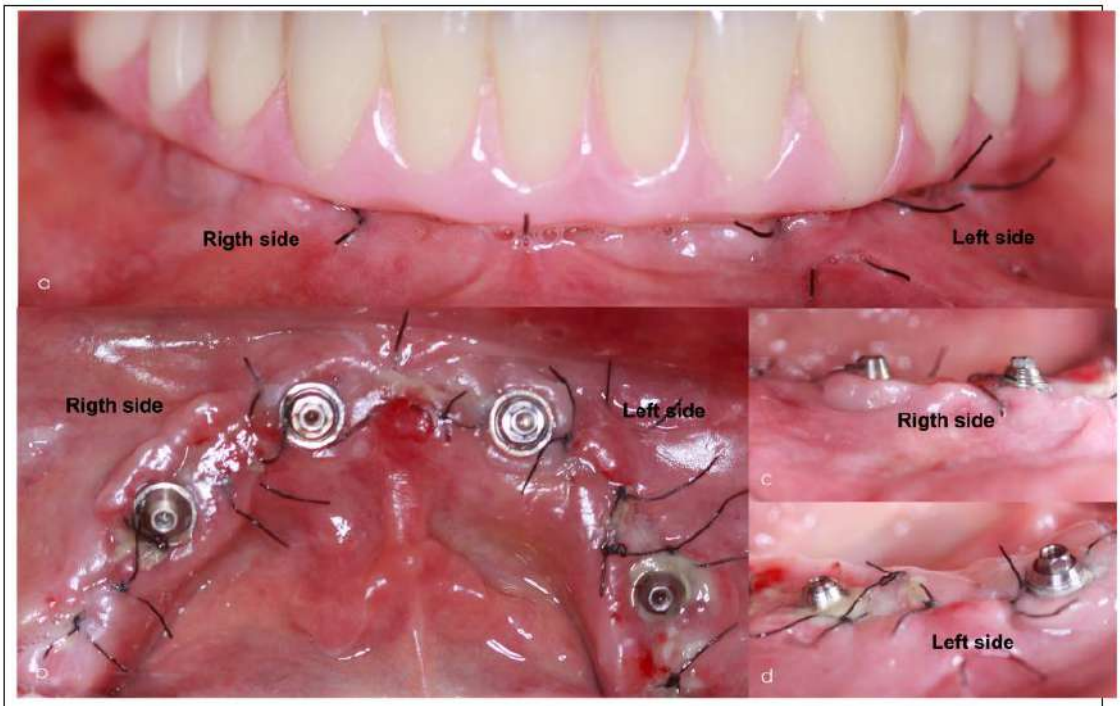

Figure 9: Patient one – 7 days postoperative. a) Image with the temporary prosthesis still in position, b) Occlusal image with the temporary prosthesis removed. It is observed that the right side that received the blue®m oral gel presents better healing, c) Lateral image on the right side, showing total closure of the flap with fine fibrin line in the interproximal area, d) Lateral image on the left side, showing closure of the flap with fibrin clot in the interproximal area.

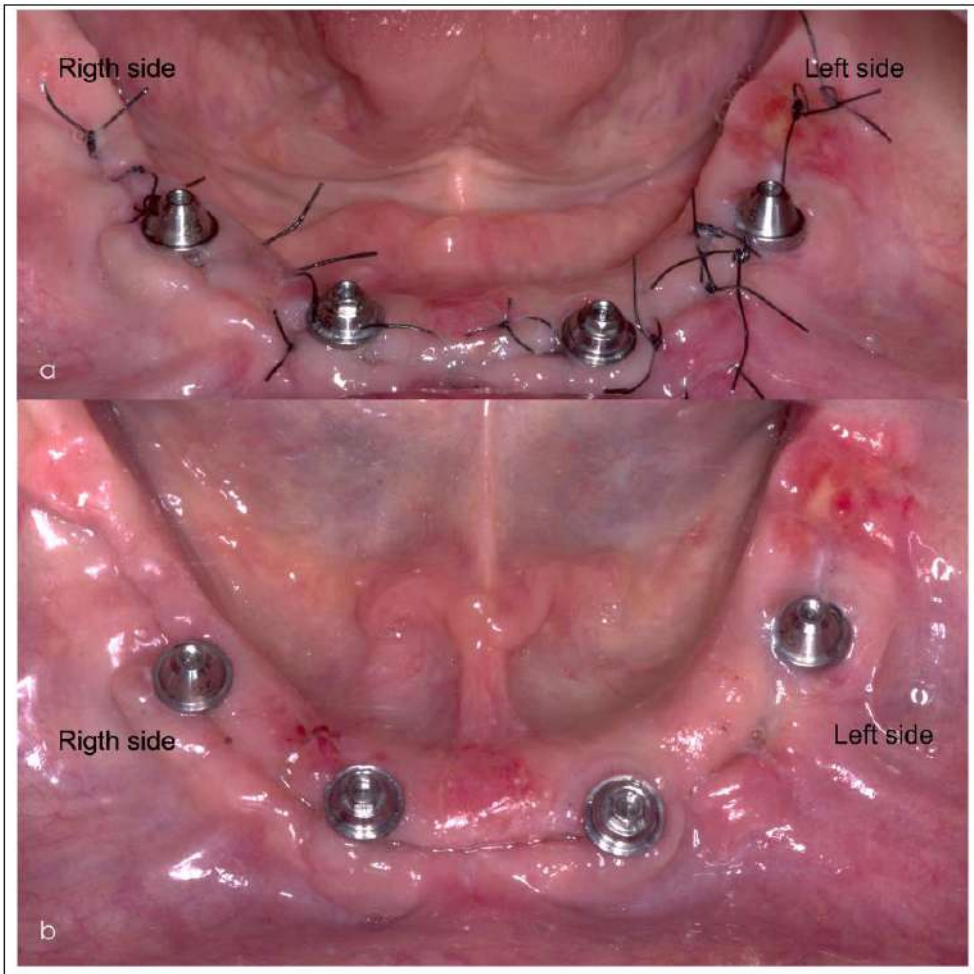

Figure 10: Patient one – 15 days postoperative. a) Image before suture removal shows the right side with better healing than the left side, b) Occlusal image after suture removal, shows the right side with total flap closure without fibrin zones and the left side shows with total flap closure with thin fibrin zones.

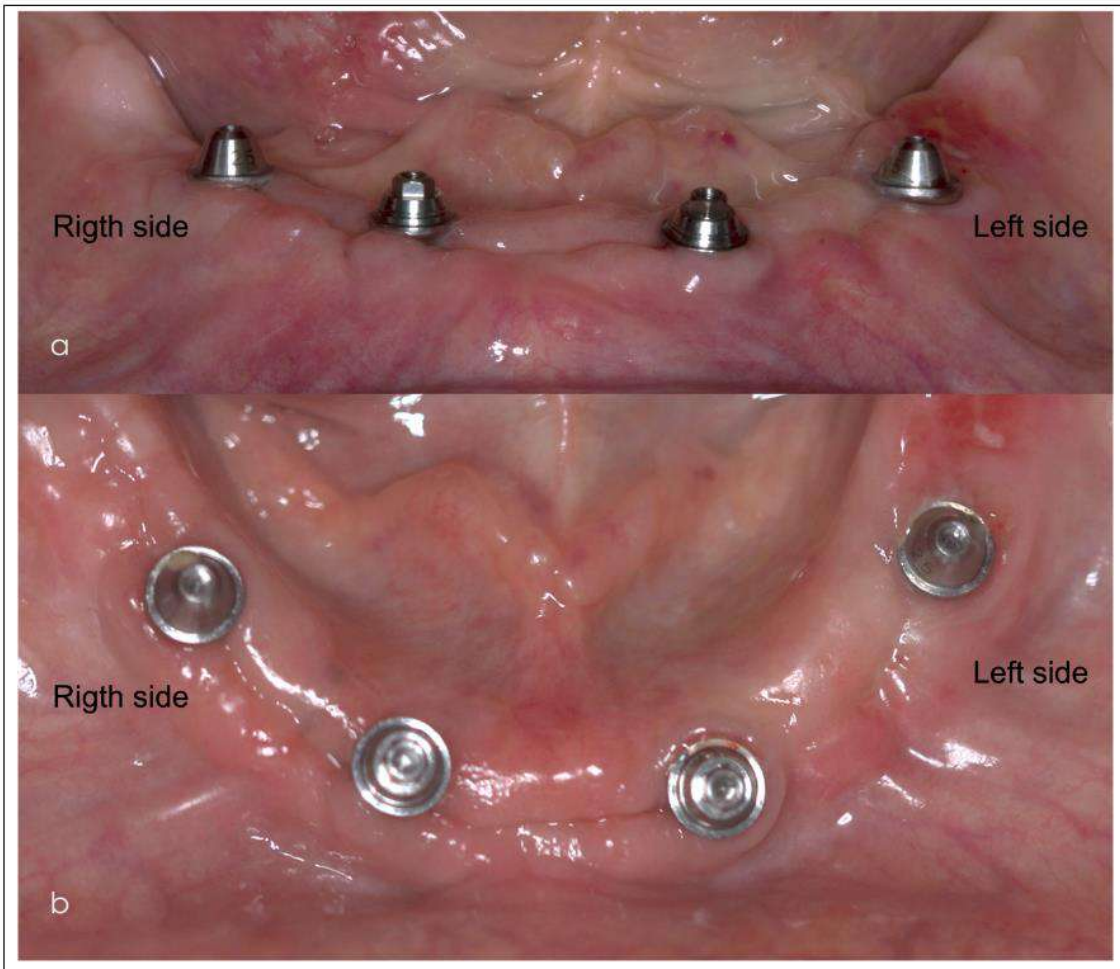

Figure 11: Patient one – 30 days postoperative. a) Frontal Image shows similar healing process between the right and left side b) Occlusal image shows the right side shows with total flap closure without fibrin zones and the left side shows with total flap closure with thin fibrin zones.

Figure 12: Patient two – 3 days postoperative. a) Right side image by buccal, shows complete flap closure with fine fibrin line in the interproximal area, b) Right side image by lingual, shows complete flap closure with fine fibrin line in the interproximal area more evident in the mesial, c) Image on the left side by buccal shows complete flap closure with fine fibrin line in the interproximal area, d) Image on the left side by lingual shows not complete flap closure with fibrin clot in the lingual and interproximal area.

Figure 13: Patient two – 7 days postoperative. a) Right side image by buccal, shows complete flap closure with fine fibrin line in the interproximal area, b) Right side image by lingual, shows complete flap closure with fine fibrin line in the interproximal area more evident in the mesial, c) Image on the left side by buccal shows complete flap closure with fine fibrin line in the interproximal area, d) Image on the left side by lingual shows not complete flap closure with fibrin clot in the lingual and interproximal area.

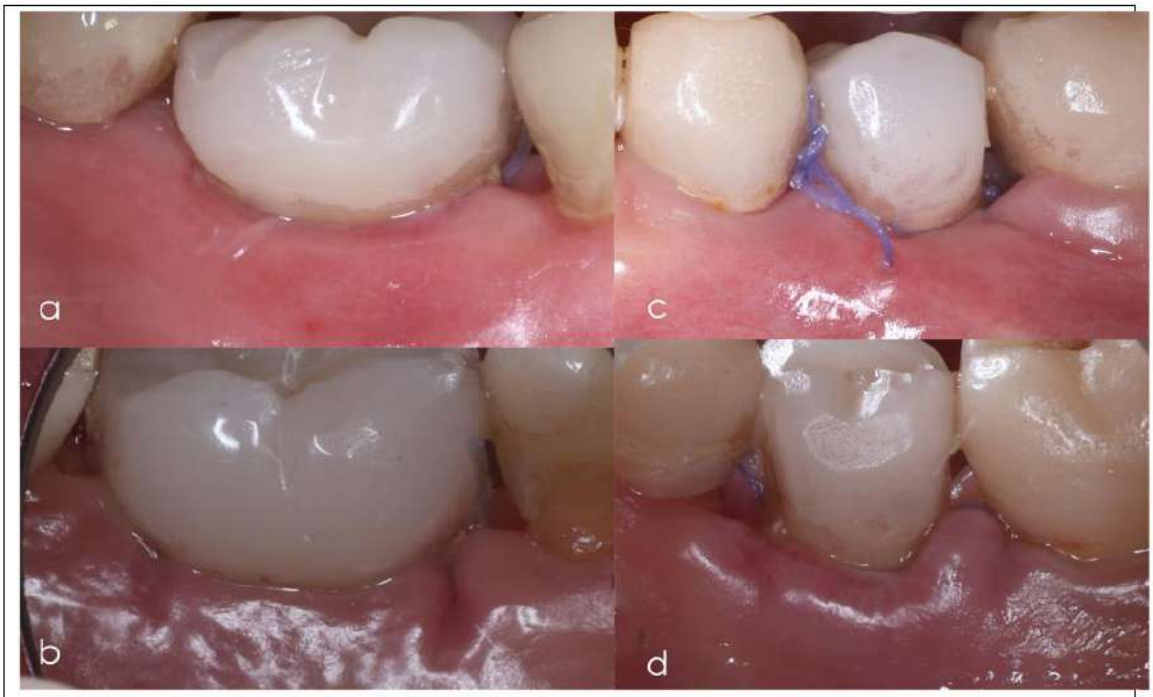

Figure 14: Patient two – 10 days postoperative. a) Right side image by buccal, shows complete flap closure and no fibrin line in the interproximal area and marginal region, b) Right side image by lingual, shows complete flap closure and no fibrin line in the interproximal area and marginal region, c) Image on the left side by buccal shows complete flap closure with fine fibrin line in the interproximal area, d) Image on the left side by lingual shows not complete flap closure fine fibrin line in lingual and the interproximal area.

Figure 15: Patient two – 15 days postoperative. Better healing was observed on the right side a) Right side image by buccal, shows complete flap closure and no fibrin line in the interproximal area and marginal region, b) Right side image by lingual, shows complete flap closure and no fibrin line in the interproximal area and marginal region, c) Image on the left side by buccal shows complete flap closure with fine fibrin line in the interproximal area, d) Image on the left side by lingual shows not complete flap closure fine fibrin line in lingual and the interproximal area.

Figure 16: Patient two – 30 days postoperative. a) Right side image by buccal, shows total flap closure without fibrin, b) Right side image by lingual, shows total flap closure without fibrin, c) Image on the left side by buccal with total closure of the flap and fibrin line marginal to the crown with the presence of inflammation due to bacterial biofilm, d) Image on the left side by lingual shows total closure of the flap and fibrin line marginal to the crown.

Figure 17: Patient two – 60 days postoperative. a) Right side image by buccal, shows complete flap closure and no fibrin line with excellent healing observed in the region, b) Right side image by lingual, shows complete flap closure and no fibrin line, c) Image on the left side by buccal shows complete closure of the flap with incomplete formation of the distal papillae, d) Image on the left side by lingual shows complete closure of the flap and no fibrin line.

Formulário 4
Avaliação da Satisfação do Demandante

Curitiba, 26 de abril de 2024.

Nº DO PROJETO	CURSO RESPONSÁVEL (MP; DP)
XX/20XX	**MP**

14. Dados do Demandante

1. Nome:	**BLUEM BRASIL S.A.**
2. CNPJ ou CPF:	26.469.621/0001-02
3. Endereço completo:	Rua México 854, sala 02, Curitiba/PR
4. Pessoa de contato:	Tatiana Deliberador
5. Telefone de contato:	41 999764948
6. E-mail de contato:	academico.cientifico@bluem.com.br

15. Satisfação com o relatório final

Quesito	**Muito Insatisfeito**	**Insatisfeito**	**Indiferente**	**Satisfeito**	**Muito Satisfeito**
	😖	😩	😐	😀	😁
Clareza do texto					X
Qualidade do vernáculo					X
Qualidade das figuras					X
Qualidade das Tabelas					X
Clareza na exposição dos resultados					X
Qualidade da Discussão					X
Qualidade Técnica Geral do Relatório					X

16. Impacto do Relatório

Quesito	Muito Improvável	Improvável	Indiferente	Provável	Muito Provável
	😖	😩	😐	😀	😁
Os resultados obtidos promoveram reflexão em algum setor da empresa?		X			
Os resultados obtidos alteraram algum procedimento da empresa?		X			
Os resultados obtidos podem impactar o lucro da empresa?				X	
Tempo de execução do projeto					

17. Interface com a equipe técnica do ILAPEO – NÃO SE APLICA

Este relatório se refere a casos clínicos realizados fora do Brasil pela aluna da faculdade ILAPEO Reyna María Ocegueda Estrada. Os casos foram realizados no consultório particular da aluna.

Quesito	Muito Insatisfeito	Insatisfeito	Indiferente	Satisfeito	Muito Satisfeito
	😖	😩	😐	😀	😁
Qualidade científica e tecnológica da equipe técnica					
Comprometimento da equipe					
Facilidade de relacionamento com a equipe					
Presteza na realização das					

atividades planejadas					

18. Descreva os impactos efetivos e/ou potencias do resultado do projeto para a empresa, explicando de que modo os resultados serão utilizados.

18.1. Particularmente informe se o resultado será incluído em dossiê para registro de produto, se apoiará a tomada de decisão pelo gestor, mudanças no processo produtivo, de marketing, de vendas e/ou treinamento.

OS RESULTADOS DOS CASOS CLINICOS APRESENTADOS MOSTRAM QUE O USO DO GEL ORAL DA BLUEM MELHORA O PROCESSO DE CICATRIZAÇÃO EM ÁREAS CIRÚRGICAS QUE RECEBERAM IMPLANTES DENTÁRIOS – FAVORECENDO A CICATRIZAÇÃO LOCAL DE FORMA MAIS RÁPIDA

19. Informe quaisquer aspectos positivos ou negativos do relatório.

NÃO TEM ASPECTOS NEGATIVOS. OS ASPECTOS POSITIVOS SÃO:

- CASOS CLÍNICOS BEM DOCUMENTADOS E QUE PODEM SER USADOS PELA EMPRESA PARA MOSTRAR A EFEITIVA CLÍNICA, NO PROCESSO DE CICATRIZAÇÃO APÓS A INSTALAÇÃO DE IMPLANTES, DO GEL ORAL DA BLUEM

TATIANA MIRANDA DELIBERADOR

_____

Responsável pela avaliação

Empresa/Setor

Responsável Acadêmica e Científica da bluem Brasil