Artigo Original

Neo-osteogenesis using an intentionally exposed polypropylene membrane after tooth extraction versus guided bone regeneration technique: A single-blind randomized controlled trial

Neo-osteogénesis utilizando una membrana de polipropileno expuesta intencionalmente después de la extracción del diente versus técnica de regeneración ósea guiada: ensayo clínico aleatorizado ciego

Neo-osteogênese utilizando uma membrana de polipropileno exposta intencionalmente após extração dentária versus técnica de regeneração óssea guiada: ensaio clínico randomizado e cego

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ABSTRACT

Introduction: The intentionally exposed polypropylene (PP) membrane has been proposed for guided bone regeneration (GBR) of the alveolar bone after extraction; however, there are biological limitations to this proposal. This study aimed to describe the effects of the PP membrane on neo-osteogenesis after tooth extraction, comparing to intentionally exposed and primary soft tissue coverage techniques. **Methodology**: This clinical trial followed the TIDieR checklist and guide. Clinical and histological parameters of alveolar repair were compared between groups: 1 (control group), without regenerative procedure; 2, GBR; and 3, intentionally exposed membrane. **Results**: Group 3 showed slight effect on the quality of new bone, compared to the control group. Although the GBR was underestimated by the early exposure of the membrane, alveolar repair and newly formed bone were superior to the other groups. Polypropylene membrane intentionally exposed compromised the volume density of the immature and mineralized bone matrix, the osteoblast and osteocyte count, and stimulated the granulation tissue formation and local inflammatory infiltrate. **Conclusions**: Despite the exposure of the PP membrane in GBR, this technique improved the quality of new bone and alveolar repair compared to the surgical technique of intentional exposure and alveolus only sutured. **Descriptors:** Polypropylenes, guided tissue regeneration, bone regeneration, tooth socket, alveolar ridge augmentation.

RESUMEN

Introducción: La membrana de polipropileno (PP) intencionalmente expuesta ha sido propuesta para la regeneración ósea guiada (GBR) del hueso alveolar después de la extracción; sin embargo, existen limitaciones biológicas a esta propuesta. Este estudio tuvo como objetivo describir los efectos de la membrana de PP en la neo-osteogénesis después de la extracción del diente, en comparación con las técnicas de cobertura de tejido blando primarias y expuestas intencionalmente. **Metodología**: Este ensayo clínico siguió la lista de verificación y la guía TIDieR. Se compararon los parámetros clínicos e histológicos de la reparación alveolar entre los grupos: 1 (grupo control), sin procedimiento regenerativo; 2, GBR; y 3, membrana expuesta intencionalmente. **Resultados:** el grupo 3 mostró un ligero efecto sobre la calidad del hueso nuevo, en comparación con el grupo de control. Aunque la GBR fue subestimada por la exposición temprana de la membrana, la reparación alveolar y el hueso neoformado fueron superiores a los otros grupos. La membrana de polipropileno expuesta intencionalmente comprometió la densidad de volumen de la matriz ósea inmadura y mineralizada, el recuento de osteoblastos y osteocitos,

ISSN 1808-5210 (Online)
ISSN 1679-5458 (Linking)

y estimuló la formación de tejido de granulación y el infiltrado inflamatorio local. **Conclusiones**: A pesar de la exposición de la membrana de PP en GBR, esta técnica mejoró la calidad del hueso nuevo y la reparación alveolar en comparación con la técnica quirúrgica de exposición intencional y alvéolo solo suturado.**Descriptores:** Polipropilenos, regeneración tisular guiada, regeneración ósea, alveolo dental, aumento de reborde alveolar.

RESUMO

Introdução: A membrana de polipropileno (PP) intencionalmente exposta tem sido proposta para regeneração óssea guiada (ROG) do osso alveolar após exodontia; no entanto, existem limitações biológicas a esta proposta. Este estudo teve como objetivo descrever os efeitos da membrana de PP na neo-osteogênese após a extração dentária, comparando com as técnicas de exposição intencional e cobertura primária de tecidos moles. **Metodologia**: Este ensaio clínico seguiu a lista de verificação e o guia TIDieR. Parâmetros clínicos e histológicos do reparo alveolar foram comparados entre os grupos: 1 (grupo controle), sem procedimento regenerativo; 2, GBR; e 3, membrana intencionalmente exposta. **Resultados**: O Grupo 3 apresentou leve efeito na qualidade do novo osso, em comparação com o grupo controle. Embora o GBR tenha sido subestimado pela exposição precoce da membrana, o reparo alveolar e o osso neoformado foram superiores aos outros grupos. A exposição intencional da membrana de polipropileno comprometeu a densidade volumétrica da matriz óssea imatura e mineralizada, a contagem de osteoblastos e osteócitos e estimulou a formação de tecido de granulação e infiltrado inflamatório local. **Conclusões**: Apesar da exposição da membrana PP na ROG, esta técnica melhorou a qualidade do novo osso e da reparação alveolar em comparação com a técnica cirúrgica de exposição intencional e alvéolo apenas suturado. **Descritores:** Polipropilenos, regeneração tecidual guiada, regeneração óssea, alvéolo dentário, aumento do rebordo alveolar.

INTRODUCTION

Tooth extraction results in atrophy and progressive loss of volume of the alveolar ridge due to the loss of function associated with an intense process of tissue remodeling. This condition compromises prosthetic rehabilitation, for which different surgical protocols for alveolar ridge preservation, both in thickness and in height, have been proposed[1-3].

Guided bone regeneration (GBR) is widely used for alveolar ridge preservation and bone reconstructions, varying the technique and type of membrane used3. GBR was initially proposed by Hurley et al. (1959), based on biological concepts and surgical techniques of guided tissue regeneration (GTR) of the supporting periodontal tissues[4]. The ideal membrane for GBR must be biocompatible, permeable to biomolecules and osteogenic cells, integrate with host tissues, be easy to use and capable of maintaining the space corresponding to the desired bone regeneration (osteopromotion property)[5,6].

The membranes isolate fibroblasts and epithelial cells from the post-extraction cavity and from the local blood clot, responsible for biological events involved in bone repair. Thus, GBR prevents the soft tissue wound healing and favors bone neoformation[6-9]. GBR presupposes the use of the subperiosteal membrane, completely covered by a stable mucoperiosteal flap and free of traction and compression forces capable of displacing the pedicle, exposing the membrane or interfering with its shape or position[10,11]. Insufficient vascularization of the pedicle is also a cause of failure in the GBR[12,13].

Resorbable collagen membranes have a lower risk of postoperative complications and technique failure compared to non-resorbable membranes[9]; however, non-resorbable barriers such as expanded and dense polytetrafluoroethylene (e- and d-PTFE) membranes, have been studied for alveolar bone reconstruction and other conditions requiring a longer period of osteopromotion[9,14-16]. A group of Brazilian researchers developed a polypropylene (PP) membrane (BoneHeal®) with the proposal to regenerate the alveolar bone after tooth extraction, keeping the membrane intentionally exposed in the initial stages of repair. BoneHeal® was characterized as a biocompatible, non-resorbable and impermeable product. Less morbidity, greater postoperative comfort and reduced risks and surgical complications were described as the main advantages of using this material[17-19].

The PP membrane retains the clot in contact with its rough surface for a period of seven to 15 days, acting as a physical barrier responsible for occlusion, clot retention and blocking cell migration from the epithelium and connective tissue to the alveolar socket[17-19]. Although the authors describe this technique as GBR, we consider that there are differences and inconsistencies in relation to the technical and biological basis of GBR, respectively[20-22]. In addition, the differences in neo-osteogenesis between the PP membrane intentionally exposed and the GBR techniques have not been investigated. Therefore, the present study aimed to describe the effects of the PP membrane on neo-osteogenesis after tooth extraction, comparing intentional exposure and primary soft tissue coverage techniques.

METHODOLOGY

STUDY DESIGN

This single-blind randomized controlled study followed the TIDieR checklist and guide[23]. The research attended the Declaration of Helsinki adopted in 1964 and seven altered versions (current, 2013), and the participants signed a Free and Informed Consent Form, based on CNS Resolution No. 466/2012. The study protocol was approved by the Research Ethics Committee of Federal University of Rio de Janeiro under No. 2.225.378.

PARTICIPANTS

Four patients with indication for extraction of at least three residual teeth or roots were included in the study. Each tooth extraction was randomly selected for the type of intervention: Group 1, minimally traumatic extraction technique (control); Group 2, minimally traumatic extraction technique associated with buccal and lingual/palatal periosteal detachment for insertion of PP membrane [BoneHeal® (BoneHeal® Ind. And Com. Ltda, Sacomã, SP, Brazil)] ends, and coronal advanced flap for primary closure and full membrane coverage for up to 4 months (primary soft tissue coverage); and Group 3, minimally traumatic extraction technique associated with PP membrane [BoneHeal® (BoneHeal® Ind. And Com. Ltda, Sacomã, SP, Brazil)] intentionally exposed for 14 days. As an exception, only groups 1 and 3 could occur in the same quadrant. The confounding factors inherent to the individual were controlled in the study due to the paired intergroup comparisons.

- Inclusion criteria: i- healthy individuals, non-smokers, 25 to 50 years old with indication of extraction of at least three teeth, in a region of D3 bone type (Misch, 2005) (24); and ii- height of the alveolar bone ≥ 12 mm in the extraction regions, assessed in cone beam computed tomography (CBCT).

- Exclusion criteria: i - hypersensitivity to polypropylene or any of the drugs prescribed in the study [e.g., amoxicillin, dexamethasone, paracetamol (acetaminophen) and chlorhexidine]; ii - inability to perform plaque control and adequate postoperative care; iii - participants with congenital syndrome affecting teeth and/or periodontal tissues, or associated with bone pathologies of the jaws; iv- pregnant or breastfeeding patients; v- chronic use of anticoagulants, immunomodulators, glucocorticoids, nonsteroidal anti-inflammatory drugs or analgesics, and bisphosphonates; vi - local odontogenic infection; vii - complex extractions with osteotomy; viii - indications for sedation or general anesthesia.

CLINICAL/SURGICAL PROCEDURES

PREOPERATIVE PATIENT PREPARATION

Initially, dental caries management, restorations requiring replacement, plaque and dental calculus remove were performed; all participants also received pre and postoperative oral hygiene guidelines. In this stage (T0), periapical radiographs and CBCT of the regions of interest were performed. Preoperative prescription: i - amoxicillin 2 g cap po one hour before surgery; e ii - dexamethasone 4 mg tab po two hours before surgery.

SURGICAL PROCEDURES

Immediately before the surgical procedure, a mouthwash with 15 ml/min 0.12 % chlorhexidine (Perioxidin®, Lacer GlaxoSmithKline Brasil, Rio de Janeiro-RJ, Brazil) was used. Then, local anesthesia was performed using 2 % lidocaine hydrochloride with epinephrine 1:200,000 (Alphacaine® 100, DFL, Rio de Janeiro, RJ, Brazil) for local anesthesia.

The three groups were operated at the same time: Group 1, minimally traumatic extraction technique + saline irrigation [20 mL of sterile 0.9 % sodium chloride solution (Cristália©, Rio de Janeiro, RJ, Brazil)] + "X" suture with 4-0 needled silk thread (Ethicon®, Inc. Johnson & Johnson©, New Brunswick, NJ, USA); Group 2, minimally traumatic extraction technique associated with buccal and lingual/palatal periosteal detachment for insertion of PP membrane ends, and coronal advanced flap for primary closure and full membrane coverage for 4 months + simple interrupted sutures with 4-0 needled silk thread (Ethicon®, Inc. Johnson & Johnson©, New Brunswick, NJ, USA); and Group 3, minimally traumatic extraction technique associated with buccal and lingual/palatal periosteal detachment for insertion of the ends of the PP membrane for 14 days + "X" suture with 4-0 needled silk thread (Ethicon®, Inc. Johnson & Johnson©, New Brunswick, NJ, USA) to retain the PP membrane intentionally exposed and maintain the stability of the buccal and lingual/palatal mucosa. Alveolar curettage and digital compression of the alveolar socket were not performed.

POSTOPERATIVE CARE

Postoperative prescription: i- mouthwash with 15 mL/min 0.12 % chlorhexidine (Perioxidin®, Lacer GlaxoSmithKline Brasil, Rio de Janeiro-RJ, Brazil) bid for seven days; ii- amoxicillin 500 mg cap po tid for seven days; ii- dexamethasone 8 mg and 4 mg tab po 24 and 48 hours after surgery, respectively;

ISSN 1808-5210 (Online)
ISSN 1679-5458 (Linking)

e iii- paracetamol (acetaminophen) 750 mg tab po qid for three days or as a rescue analgesic.

RESULTS

The follow-up was carried out twice a week in the first 30 days after the surgery and every 15 days from the 31st to the 60th day after the surgery. Four months after surgery, the imaging exams were updated and the collection of a local bone fragment (biopsy) for histological analysis of the newly formed tissue was performed immediately before the installation of the dental implants [Timeline (Figure 1)].

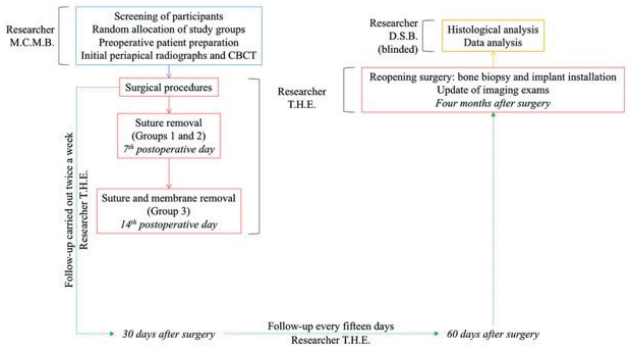

Figura 1 - Timeline.

Cases 1, 2, 3 and 4 were 37, 50, 40 and 29 years old and only one participant was female (Case 4). Of the four study participants, Case 4 did not attend all scheduled clinical follow-up visits.

In group 2, the coronal advanced flap allowed full coverage of the PP membrane. Both membrane and pedicle remained stable and free from traction and compression forces in the immediate postoperative period. Despite the correct execution of the surgical technique, exposure of the PP membrane occurred in the first eight postoperative days in Group 2 in all cases, associated with flap dehiscence and intense inflammation of the pedicle, with no clinical signs of infection in the operated area. In these cases, the membrane was removed. The clinical aspect of the repair was similar in groups 2 and 3 14 days after surgery, except for the remodeling of the vestibular tissue in Group 2 related to the pedicle.

The late local tissue repair showed characteristics of normality in the three groups studied: normochromic and keratinized mucosa over the remaining alveolar ridge and absence of clinical signs or symptoms of inflammation or infection.

The clinical evaluation of the initial stages of local tissue repair was classified as: i- closure of the surgical wound, categorized as "complete" or "open" (absence or presence of granulation tissue or connective tissue evident in the extraction area, respectively); color of oral mucosa, categorized as "normochromic" tissue (compatible with normality), "reddish" (inflamed tissue) or "whitish" (clinical sign of infection or necrosis); iii- digital texture analysis of the mucosa, categorized as "firm" (characteristic of the keratinized and inserted mucosa) or "soft" (characteristic of the lining mucosa, not keratinized and not attached); and iv- position of the mucogingival line, classified as "without alteration", "slightly displaced to the crest", "slightly displaced to the lingual/palatal region" and "displaced to the lingual/palatal region". Four months after surgery, there was a displacement of the mucogingival line towards the alveolar bone crest in cases 1 and 3, only in Group 2 (Table 1).

Table 1 - Descriptive clinical parameters of the local mucosa four months after surgery.

	Clinical parameters	Group 1	Group 2	Group 3
Case 1	Closure of the surgical wound	"complete"	"complete"	"complete"
	Color of oral mucosa	"normochromic"	"normochromic"	"normochromic"
	Digital texture analysis of the mucosa	"firm"	"firm"	"firm"
	Position of the mucogingival line	"without alteration"	"slightly displaced to the crest"	"without alteration"
Case 2	Closure of the surgical wound	"complete"	"complete"	"complete"
	Color of oral mucosa	"normochromic"	"normochromic"	"normochromic"
	Digital texture analysis of the mucosa	"firm"	"firm"	"firm"
	Position of the mucogingival line	"without alteration"	"without alteration"	"without alteration"
Case 3	Closure of the surgical wound	"complete"	"complete"	"complete"
	Color of oral mucosa	"normochromic"	"normochromic"	"normochromic"
	Digital texture analysis of the mucosa	"firm"	"firm"	"firm"
	Position of the mucogingival line	"without alteration"	"slightly displaced to the crest"	"without alteration"

The complete filling of the socket by newly formed bone, observed in imaging exams, was confirmed during the reopening surgery for biopsy and implant installation. Biopsies were collected immediately before the dental implants were installed, using a 2 mm diameter trephine drill, deepening 10 mm in the newly formed alveolar bone. The samples were stored in vials containing 10 % buffered formic aldehyde (phosphate buffer) in a 1:10 volumetric ratio, and identified by the researcher T.H.E. using numeric codes, to guarantee the masking (blinding) of the researcher D.S.B. responsible for the analysis of photomicrographs.

The quality of the newly formed bone was assessed by histological analysis. The bone biopsy of one participant (Case 3) was disregarded due to impaired sample integrity in at least one of the three groups studied. The photomicrographs of Groups 1, 2 and 3 stained with hematoxylin and eosin and Picro Sirius are shown in Figure 2.

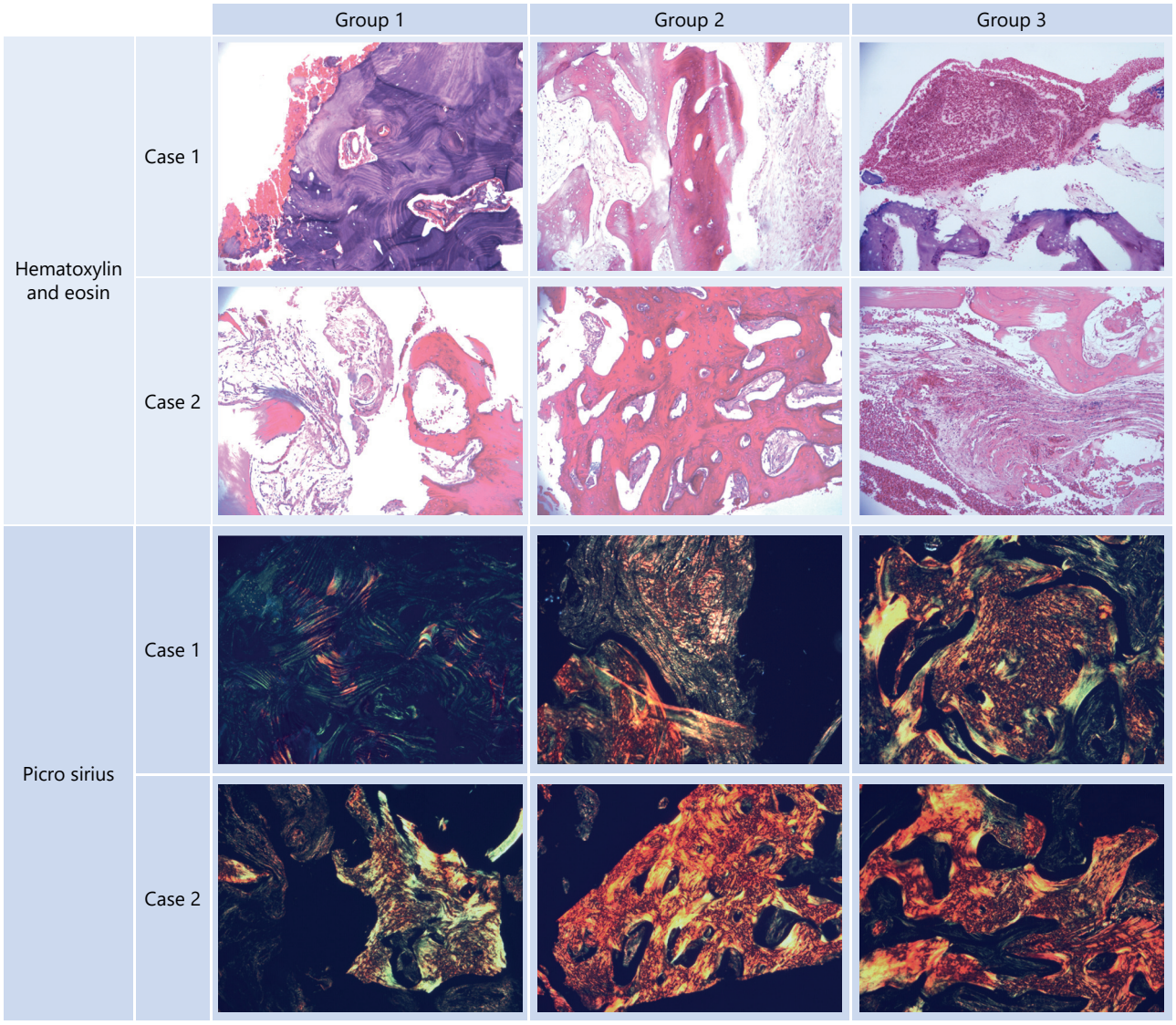

Figura 2 - Photomicrographs of the three groups studied in Cases 1 and 2.

Footnote: The biopsies were decalcified in 10 % disodium ethylene diamine tetraacetic solution (EDTA) (EDTA, PA, Poquímios®, Rio de Janeiro, RJ, Brazil) pH 7.0. The samples were submitted to paraffin processing; after the inclusions, 5 mm thick cuts were performed. The tissues adhered to the glass slides were stained with hematoxylin and eosin and Picro Sirius for analysis under light optical microscopy and polarized light microscopy, respectively. Picro Sirius analysis: i- green, immature collagen tissue; ii- yellow, partially mature collagen tissue; and iii- red, mature collagen tissueAll micrographs were captured and stored in JPEG format (24-bit color, 640x512 pixels) using a camera (Olympus® BX51/LC Evolution) connected to the microscope (Carl ZEISS®, Jena, Germany). Total magnification = 100X (10X objective and 10X ocular).

Histological analysis was performed on the most coronal portion of the bone fragment. The presence of a blood clot was observed in groups 1 and 3, being more evident in Group 3. The amount of neo-deposited and mineralized bone was more significant in groups 1 and 2. Primary soft tissue coverage over the PP membrane (Group 2) resulted in better neo-osteogenesis and less inflammatory infiltrate, compared to Group 3. Polarized light microscopy showed a greater

ISSN 1808-5210 (Online)
ISSN 1679-5458 (Linking)

amount of mature collagen matrix in the Group 3; this result did not represent a greater amount of newly formed bone (Table 2).

Table 2 - Stereological analysis of newly formed bone biopsies.

	Case 1	Case 2
Group 1	Blood clot – 14 % Newly deposited bone matrix (immature bone) – 44 % Mineralized bone matrix – 28 % Osteoblast rhymes – 3 % Osteocytes – 0 % Osteoblasts – 3 % Granulation tissue – 0 % Capillar – 3 % Inflammatory infiltrate – 0 % Immature collagen – 72 % Partially mature collagen – 3 % Mature collagen – 11 %	Blood clot – 3 % Newly deposited bone matrix (immature bone) – 28 % Mineralized bone matrix – 14 % Osteoblast rhymes – 17 % Osteocytes – 0 % Osteoblasts – 31 % Granulation tissue – 11 % Capillar – 0 % Inflammatory infiltrate – 0 % Immature collagen – 28 % Partially mature collagen – 33 % Mature collagen – 6 %
Group 2	Blood clot – 0 % Newly deposited bone matrix (immature bone) – 25 % Mineralized bone matrix – 25 % Osteoblast rhymes – 6 % Osteocytes – 22 % Osteoblasts – 6 % Granulation tissue – 22 % Capillar – 0 % Inflammatory infiltrate – 3 % Immature collagen – 42 % Partially mature collagen – 22 % Mature collagen – 17 %	Blood clot – 0 % Newly deposited bone matrix (immature bone) – 11 % Mineralized bone matrix – 78 % Osteoblast rhymes – 11 % Osteocytes – 19 % Osteoblasts – 14 % Granulation tissue – 0 % Capillar – 0 % Inflammatory infiltrate – 0 % Immature collagen – 17 % Partially mature collagen – 19 % Mature collagen – 44 %
Grupo 3	Blood clot – 47 % Newly deposited bone matrix (immature bone) – 3 % Mineralized bone matrix – 6 % Osteoblast rhymes – 0 % Osteocytes – 6 % Osteoblasts – 0 % Granulation tissue – 11 % Capillar – 0 % Inflammatory infiltrate – 19 % Immature collagen – 33 % Partially mature collagen – 44 % Mature collagen – 17 %	Blood clot – 22 % Newly deposited bone matrix (immature bone) – 36 % Mineralized bone matrix – 19 % Osteoblast rhymes – 9 % Osteocytes – 0 % Osteoblasts – 9 % Granulation tissue – 14 % Capillar – 0 % Inflammatory infiltrate – 17 % Immature collagen – 19 % Partially mature collagen – 8 % Mature collagen – 61 %

Footnote: The semiquantitative analysis of the photomicrographs (stereological method - P36 system) estimated the volume density (VV) of cells and structures using the formula: VV = PP/TP [% (PP, partial points; TP, total points)]. Collagen classification: i- green, immature collagen tissue; ii- yellow, partially mature collagen tissue; and iii- red, mature collagen tissue (Picro Sirius analysis). The prevalence by area was obtained using the image segmentation technique of the Image-Pro Plus® version 5.0 program (Media Cybernetics, Silver Spring, USA). The analyzes were performed from five image captures obtained in three different histological slides [each set analyzed separately (triplicate; n = 5 x 3 = 15 images per group)].

METHODOLOGY

The PP membrane was reported as a biocompatible material suitable for GBR, especially for dental socket after extraction[17-19]. However, the intentional exposure technique proposed contradicts the technical and biological basis of GBR[5-12,20-22].

The two surgical techniques tested for bone regeneration improved alveolar bone neoformation, compared to the control group (Group 1). Our results suggest that, despite early exposure of the PP membrane, the GBR technique with primary soft tissue coverage over the PP membrane showed better neo-osteogenesis in relation to the intentional exposure technique.

Although the surgical technique was well performed by an experienced surgeon, the elastic shape memory of the membrane, and the dimensional changes of the mucosa due to the natural accommodation of the pedicle and decreased swelling may have contributed to the early exposure of the PP membrane in Group 2[5-9,20,25]. This postoperative complication suggests that the biocompatibility of the tested membrane has limitations for other surgical techniques and should be used mainly for intentional exposure for 7-15 days[5,6,9,20]. There is no evidence on the effectiveness of PP membrane in GBR (primary soft tissue coverage over the membrane).

The mucogingival line slightly displaced to the crest was expected in Group 2, as the advanced coronal flap for full membrane coverage alters the local oral vestibule and the contour of the mucogingival line[26]. In this context, non-resorbable membranes intentionally exposed have the potential to increase local keratinized tissue, representing an advantage of the technique[27]. At the 4-month follow-up, the operated areas were also healthy, with no clinical signs or symptoms of inflammation.

The use of PP membrane intentionally exposed for post-extraction socket[17-19] is supported by previous studies using d-PTFE membrane; however, the surgical protocols are different28. The intentional exposure of non-resorbable barriers without primary closure, such as PP and d-PTFE membranes, favors minimal flap dissection and preservation of the interdental papillae and keratinized mucosa. The impermeability of these materials reduces the risk of local bacterial infection, adding to the effect of the systemic antibiotic[28]. Although the PP membrane must be removed between the seventh and the 15th postoperative day[17-19], removal of the d-PTFE membrane has been reported four to six weeks after surgery[28]. According to the authors, this period is sufficient for the formation of a well-consolidated layer of osteoid or bone tissue under the d-PTFE membrane; epithelialization over osteoid tissue is completed 10 to 14 days after removal of the membrane. As established in this study, the authors recommend reopening surgery for biopsy and implant installation four months after regenerative surgery[28].

The PP membrane intentionally exposed for 14 days was associated with a higher volume density of blood clot, granulation tissue and inflammatory infiltrate than groups 1 and 2 and did not favor the presence of osteoblasts and osteocytes. There were slight benefits from the intentional exposure technique compared to the control group. These findings suggest limitations of the technique compared to GBR, with regard to stability, being biocompatible with tissue integration, being able to create and maintain space, and being occlusive with selective permeability[5-13,20-22,29]. In GBR, the primary closure and full membrane coverage protect and guarantee the stability of the membrane, which is not the case with the intentional exposure technique. Thus, local stimuli can interfere with the mechanical regulation of bone regeneration, leading to the formation of fibrous connective tissue or new bone of low quality[30]. Apparently, the retention of the blood clot on the rough surface of the PP membrane (BoneHeal®) was not sufficient for bone regeneration in the face of these limitations.

In addition to the bone regeneration time mediated by the PP membrane, the non-association of this technique with bone graft or dental implant to alveolar ridge preservation may explain the different results compared to studies on d-PTFE without primary closure[28].

This series of cases reinforces the conceptual hypothesis that the intentional exposure technique does not represent a GBR procedure and does not present the same results. Barber et al. (2007) described the use of the d-PTFE membrane without primary closure for alveolar ridge preservation and bone regeneration but did not define this technique as GBR[28].. The biological mechanisms and surgical requirements related to GBR have been established and are continuously updated. Although the development of new techniques and new materials should be encouraged, this process must always be supported by biological principles and previous clinical evidence.

The main limitations are inherent to the study design, such as the level of evidence of the reported findings. It is not possible to affirm a causal relationship between the surgical approaches studied and the quality of the newly formed bone, nor what is the best technique for preserving the alveolar ridge; randomized controlled trials are needed to answer the questions raised in this study and to guide clinical decision-making. Even so, this study represents an important contribution to clinical practice and the design of new studies, for the critical review of the biological bases of bone regeneration and the concept of GBR applied to intentional exposure technique.

CONCLUSIONS

Clinical and histological analyzes suggest the limited use of PP for GBR, and that PP membrane intentionally exposed did not represent a significant improvement in the quality of the new bone, compared to only suture. In addition, the GBR surgical technique, even compromised by early exposure of the membrane, showed better quality of the new bone than the other groups.

ISSN 1808-5210 (Online)
ISSN 1679-5458 (Linking)

ACKNOWLEDGMENTS

The authors acknowledge the financial support provided by the following Brazilian funding agencies: Coordination for the Improvement of Higher Education (CAPES), National Council for Scientific and Technological Development (CNPq) and Science and Technology Support Foundation of the State of Pernambuco (FACEPE). We are also grateful to the Federal University of Rio de Janeiro (UFRJ) and Federal University of Pernambuco (UFPE) for all the support.

CONFLICT OF INTEREST DISCLOSURES

None reported.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the study and were equally important in the study design, surgeries and data analysis, review of the literature and preparation of the manuscript. All authors have reviewed this document, are responsible for its content and have agreed to its submission for publication.

ADDITIONAL CONTRIBUTIONS

We thank the patient for granting permission to publish this information.

COMPLIANCE WITH ETHICAL STANDARDS (ETHICAL APPROVAL)

This research followed the 'Declaration of Helsinki' adopted in 1964 and seven amended versions (current, 2013). The publication of this study followed the rules of 'Carta Circular 166/2018-CONEP/SECNS/MS' and was approved by the Research Ethics Committee of Federal University of Rio de Janeiro under No. 2.225.378.

FUNDING

None reported.

REFERENCES

1. Araújo MG, Lindhe J. Dimensional ridge alterations following tooth extraction. An experimental study in the dog. J Clin Periodontol. 2005;32(2):212-218. doi:10.1111/j.1600-051X.2005.00642.x.

2. Tan WL, Wong TL, Wong MC, Lang NP. A systematic review of post-extractional alveolar hard and soft tissue dimensional changes in humans. Clin Oral Implants Res. 2012;23 Suppl 5:1-21. doi:10.1111/j.1600-0501.2011.02375.x.

3. Jepsen S, Schwarz F, Cordaro L, et al. Regeneration of alveolar ridge defects. Consensus report of group 4 of the 15th European Workshop on Periodontology on Bone Regeneration. J Clin Periodontol. 2019;46 Suppl 21:277-286. doi:10.1111/jcpe.13121.

4. Hurley LA, Stinchfield FE, Bassett AL, Lyon WH. The role of soft tissues in osteogenesis. An experimental study of canine spine fusions. J Bone Joint Surg Am. 1959;41-A:1243-1254.

5. Hardwick R., Scantlebury T. V., Sanchez R., Whitley N, Ambruster J. Membrane design criteria for guided bone regeneration of the alveolar ridge. In: Buser D, Dahlin C, Schenk RK, editors. Guided bone regeneration in implant dentistry. Chicago: Quintessence: 101–136, 1994.

6. Rolvien T, Barbeck M, Wenisch S, Amling M, Krause M. Cellular Mechanisms Responsible for Success and Failure of Bone Substitute Materials. Int J Mol Sci. 2018;19(10):2893. Published 2018 Sep 23. doi:10.3390/ijms19102893.

7. Dahlin C, Linde A, Gottlow J, Nyman S. Healing of bone defects by guided tissue regeneration. Plast Reconstr Surg. 1988;81(5):672-676. doi:10.1097/00006534-198805000-00004.

8. Hämmerle CH, Jung RE. Bone augmentation by means of barrier membranes. Periodontol 2000. 2003;33:36-53. doi:10.1046/j.0906-6713.2003.03304.x.

9. Sanz M, Dahlin C, Apatzidou D, et al. Biomaterials and regenerative technologies used in bone regeneration in the craniomaxillofacial region: Consensus report of group 2 of the 15th European Workshop on Periodontology on Bone Regeneration. J Clin Periodontol. 2019;46 Suppl 21:82-91. doi:10.1111/jcpe.13123.

10. Lim G, Lin GH, Monje A, Chan HL, Wang HL. Wound Healing Complications Following Guided Bone Regeneration for Ridge Augmentation: A Systematic Review and Meta-Analysis. Int J Oral Maxillofac

Implants. 2018;33(1):41–50. doi:10.11607/jomi.5581.

11. Garcia J, Dodge A, Luepke P, Wang HL, Kapila Y, Lin GH. Effect of membrane exposure on guided bone regeneration: A systematic review and meta-analysis. Clin Oral Implants Res. 2018;29(3):328-338. doi:10.1111/clr.13121.

12. McAllister BS, Haghighat K. Bone augmentation techniques. J Periodontol. 2007;78(3):377-396. doi:10.1902/jop.2007.060048.

13. Chiapasco M, Zaniboni M. Clinical outcomes of GBR procedures to correct peri-implant dehiscences and fenestrations: a systematic review. Clin Oral Implants Res. 2009;20 Suppl 4:113-123. doi:10.1111/j.1600-0501.2009.01781.x.

14. Fu JH, Wang HL. Horizontal bone augmentation: the decision tree. Int J Periodontics Restorative Dent. 2011;31(4):429-436.

15. Tolstunov L. Surgical Restorative Decision Algorithm for Edentulous Condition in Implant Dentistry With Emphasis on Bone Augmentation. J Oral Implantol. 2019;45(5):421-424. doi:10.1563/aaid-joi-D-18-00315.

16. Misch CM, Basma H, Misch-Haring MA, Wang HL. An Updated Decision Tree for Vertical Bone Augmentation. Int J Periodontics Restorative Dent. 2021;41(1):11-21. doi:10.11607/prd.4996.

17. Munir S, Siqueira, JTTD. Uso de barreira de polipropileno pós exodontia. Relato de três casos clínicos. Rev Bras Implant. 2009;15(2) 12-5.

18. Salomão M, Alvarez FK, Siqueira JTTD. Regeneração óssea guiada em defeitos extensos pós-exodontias utilizando membrana exposta ao meio bucal. ImplantNews. 2010;753-759.

19. Salomâo M, Siqueira JTTD. Uso de barreira exposta ao meio bucal para regeneração óssea guiada após a exodontia. Rev Assoc Paul Cir Dent. 2010;184-188.

20. Retzepi M, Donos N. Guided Bone Regeneration: biological principle and therapeutic applications. Clin Oral Implants Res. 2010;21(6):567-576. doi:10.1111/j.1600-0501.2010.01922.x.

21. Elgali I, Omar O, Dahlin C, Thomsen P. Guided bone regeneration: materials and biological mechanisms revisited. Eur J Oral Sci. 2017;125(5):315-337. doi:10.1111/eos.12364.

22. Urban IA, Monje A. Guided Bone Regeneration in Alveolar Bone Reconstruction. Oral Maxillofac Surg Clin North Am. 2019;31(2):331-338. doi:10.1016/j.coms.2019.01.003.

23. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, Altman DG, Barbour V, Macdonald H, Johnston M, Lamb SE, Dixon-Woods M, McCulloch P, Wyatt JC, Chan AW, Michie S. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ. 2014 Mar 7;348:g1687. doi: 10.1136/bmj.g1687.

24. Misch CE. Bone density: A key determinant for clinical success. In: Misch CE, editor. Contemporary Implant Dentistry, 2nd ed. St Louis: CV Mosby Company; 1999. p. 109-18.

25. Silver E, Wu R, Grady J, Song L. Knot Security- How is it Affected by Suture Technique, Material, Size, and Number of Throws?. J Oral Maxillofac Surg. 2016;74(7):1304-1312. doi:10.1016/j.joms.2016.02.004.

26. Gürgan CA, Oruç AM, Akkaya M. Alterations in location of the mucogingival junction 5 years after coronally repositioned flap surgery. J Periodontol. 2004;75(6):893-901. doi:10.1902/jop.2004.75.6.893.

27. Mandarino D, Luz D, Moraschini V, Rodrigues DM, Barboza ESP. Alveolar ridge preservation using a non-resorbable membrane: randomized clinical trial with biomolecular analysis. Int J Oral Maxillofac Surg. 2018;47(11):1465-1473. doi:10.1016/j.ijom.2018.06.011.

ISSN 1808-5210 (Online)
ISSN 1679-5458 (Linking)