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Histological analysis of the use of biphasic ceramics based on hydroxyapatite and β-tricalcium phosphate in maxillary sinus floor elevation surgery: pilot study

Análise histológica do uso da cerâmica bifásica a base de hidroxiapatita e β-tricálcio fosfato em cirurgia de elevação de assoalho de seio maxilar: estudo piloto

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Resumo

Objetivo: Avaliar o reparo ósseo associado ao uso da cerâmica bifásica a base de hidroxiapatita e β-tricálcio fosfato (HA/TCP) nos procedimentos de elevação da membrana do seio maxilar em humanos. **Material e método:** Foram selecionados 10 pacientes com rebordo ósseo residual entre 3 mm e 5 mm de altura na região posterior da maxila e que tinham indicação para procedimentos de enxertia óssea associado ao levantamento de seio maxilar. Os seios maxilares foram preenchidos com HA/TCP, e após 8 meses, foi executado a instalação dos implantes e nesse momento foi realizada a coleta de um fragmento ósseo com auxílio de uma broca trefina, o qual foi submetido à análise histológica da área enxertada. **Resultado:** A análise histológica das biópsias revelou a presença de tecido ósseo vital e imaturo, justaposto ao biomaterial. A análise histomorfométrica revelou percentuais de 28,8%, 27,4% e 43,6% para tecido ósseo, biomaterial e tecido mole, respectivamente. **Conclusão:** As áreas enxertadas com a HA/TCP apresentaram quantidade adequada de formação óssea que permitiu a instalação dos implantes. O sucesso do procedimento de enxertia com esse biomaterial esteve associado ao seu potencial de osteocondução que permitiu a formação de tecido ósseo em íntimo contato com a HA/TCP.

Descritores: Seio maxilar; transplante ósseo; implantes dentários.

Abstract

Objective: To evaluate the bone repair associated with the use of biphasic ceramics based on hydroxyapatite and β-tricalcium phosphate (HA/TCP) in the procedures of maxillary sinus membrane elevation in human beings. **Material and method:** Ten patients with a residual bone ridge in the posterior maxillary region between 3 mm and 5 mm in height were selected and indicated for procedures of bone grafting associated with maxillary sinus lift procedure. The maxillary sinuses were filled with HA/TCP, and after 8 months, the implants were implanted and a bone biopsy was collected with the aid of a trephine drill, which was then submitted to histological analysis for the evaluation of the composition of the grafted area. **Result:** The histological description analysis of the biopsies revealed the presence of vital and immature bone tissue, juxtaposed to the biomaterial. Histomorphometric analysis showed that the biopsy composition was in average 28.8%, 27.4%, and 43.6% of bone tissue, biomaterial, and soft tissue, respectively. **Conclusion:** The areas grafted with HA/TCP presented the adequate amount of bone formation that allowed the implantation of the implants. The success of the grafting procedure with this biomaterial was associated with its osteoconduction potential that allowed the formation of bone tissue in close contact with HA/TCP.

Descriptors: Maxillary sinus; bone transplantation; dental implants.

INTRODUCTION

The installation of osteointegratable implants is a viable and predictable alternative for the rehabilitation of edentulous ridges. However, their high success rates are related to adequate bone availability[1,2]. The posterior maxillary region is considered a critical area for the implant installation since frequently dental extraction associated with maxillary sinus pneumatization promotes bone

resorption processes that prevent the implantation of conventional-sized implants in a suitable position[3,4] that requires procedures of bone grafting associated with the removal of the floor membrane of the maxillary sinus[4,5].

The use of the autogenous bone graft has been considered as the gold standard among the bone substitutes proposed for bone grafting procedures because it is the only biomaterial that associates the biological properties of bone formation of osteogenesis, osteoconduction, and osteoinduction[5,6]. However, limitations of the use of autogenous bone as a graft such as a discomfort and a morbidity associated with its collection[7], limited availability in the buccal cavity[6] and their reabsorption rates mainly when used in their particulate form[5,7] have stimulated the use of biomaterials of other origins[6,8].

The group of alloplastic biomaterials has been very indicated among the biomaterials as an alternative to the use of autogenous bone due to its good osteoconduction property that allows the implants and maintenance of clinical results with high survival rates[9]. Biphasic ceramics based on hydroxyapatite and β-tricalcium phosphate have been widely used in a wide variety of clinical situations such as maxillary sinus elevation[10], maintenance of post-extracting alveoli[11] and filling of defects such as dehiscences in immediate implants[12]. It has been reported that the action of this biomaterial to promote bone formation is associated with reabsorption of the β-tricalcium phosphate portion, which may induce osteoblastic differentiation, and the maintenance of hydroxyapatite, which allows the process of osteoconduction and reduction of resorption of the body of the biomaterial in comparison to alloplastic grafts constituted of pure β-tricalcium phosphate[10,13,14].

Although the clinical documentation of the use of biphasic ceramic based on hydroxyapatite and β-tricalcium phosphate has previously been described[8,10,14], it should be noted that the evaluation of the histological quality of the application of this biomaterial in maxillary sinus survey deserves further investigation because there are some variations in the proportion of hydroxyapatite and β-tricalcium phosphate that have been used clinically, and this fact may influence the results promoted by these biomaterials[10,15]. The aim of this study was to evaluate histologically the use of biphasic ceramics based on 60% hydroxyapatite and 40% β-tricalcium phosphate on procedures to elevate the maxillary sinus membrane in human beings.

MATERIAL AND METHOD

Sample Selection

Five of the ten maxillary sinuses of 6 partially edentulous patients who needed the installation of osseointegrative implants for rehabilitation in the posterior part of the maxilla, but without sufficient bone availability for their installation were selected and invited to participate in this study. These patients were grafted with hydroxyapatite (HA) and tricalcium phosphate (TCP), (Clonos® Neoortho, Curitiba, Brazil). All patients submitted to the study completed the free informed consent agreement, agreeing to participate in the study. The study was approved by the Research Ethics Committee Hospital Amaral Carvalho Foundation (protocol 1.220.146).

The inclusion criteria were dental absences in the posterior maxilla with pneumatization of the maxillary sinus and without surgical interventions for at least 6 months, patients without the systemic involvement and parafunctional habits. Also, all patients should agree to participate freely in this research.

The exclusion criteria were based on the presence of untreated sinusopathies, ASA II (controlled), III, IV or V patients, patients with a history of periodontitis, irradiated, patients with diabetes or any systemic impairment that increase repair time, presence of Underwood septa, patients who had ruptured sinus membranes during the transoperative period, pregnant patients, smokers, and those with special needs.

Surgical Procedures

All surgical procedures were performed under aseptic conditions, by the same surgeon. After local anesthesia was applied, access to the lateral wall of the maxillary sinus was performed through a mucoperiosteal flap of total thickness with an incision on the crest of the alveolar ridge, with anterior and posterior relaxing vertical incisions that were performed with sufficient length to allow good access to the surgical bed. The anthrostomy was then performed to gain access to Schneider´s membrane (Figure 1A), which was elevated (Figure 1B), promoting the creation of space that was filled with biphasic ceramic based on hydroxyapatite and β-tricalcium phosphate (Figure 1C), and finally, the flap was repositioned and sutured. The patients selected for this study were medicated in the postoperative period with an antibiotic: amoxicillin 500 mg + clavulanic acid 125 mg, 1 capsule of 8/8 hours for 07 days; anti-inflammatory: nimesulide 100 mg, 1 tablet of 12/12 hours for 03 days and analgesic: dipyrone sodium 500 mg, 01 tablet of 06/06hours in case of pain. If the patient is sensitive to some of these substances, clindamycin 300 mg: 1 8/8 hours tablet for 7 days, ibuprofen 600 mg: 1 8/8 hours tablet for 03 days and paracetamol 750 mg: 1 6/6 hours tablet in case of pain.

After 8 months, a computerized tomography was used to measure the gain of mineralized tissue and to plan the implant installation (Figure 2). During the second surgical procedure, procedures of asepsis, anesthesia and flap opening were performed similarly to those performed in the procedure of lifting the maxillary sinus membrane. Before implants, a biopsy was performed with the aid of a trephine drill with a 3.3 mm internal diameter in the lateral wall of the grafted maxillary sinus (Neodent®, Curitiba, Brazil) (Figure 1D). Subsequently, the implants were installed and the suture was performed. The postoperative care was similar to the first surgical procedure

Histological Processing and Histological/ Histomorphometric Analysis

After collection, specimens were fixed in 10% buffered formalin for 24 hours, washed in running water for 12 hours and demineralized in 9% EDTA solution at pH 7.0 for 40 days. The pieces were subsequently dehydrated in alcohol 70%, 80%, 95%

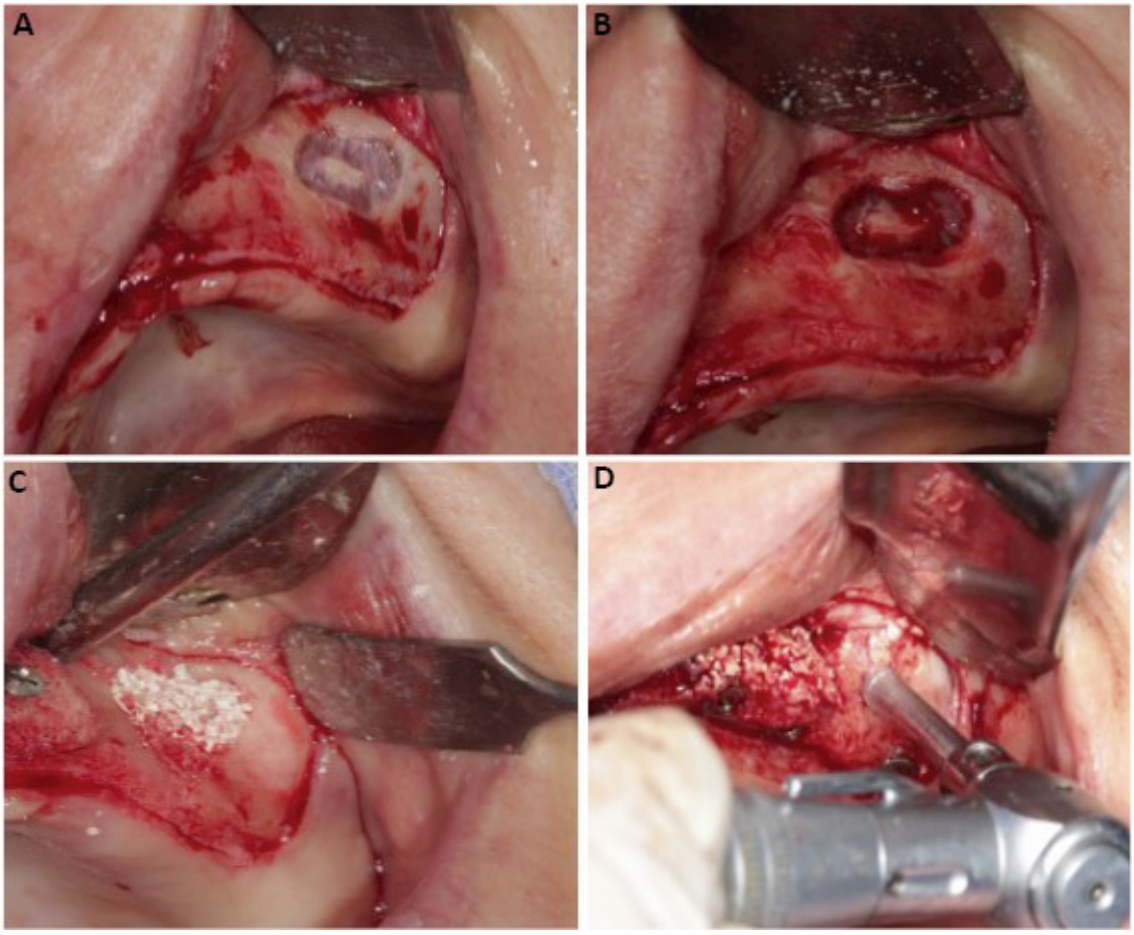

Figure 1. Exposure (A) and elevation (B) of the sinus membrane, insertion of the biomaterial (C). After 8 months of grafting procedures, collection of the bone fragment (D).

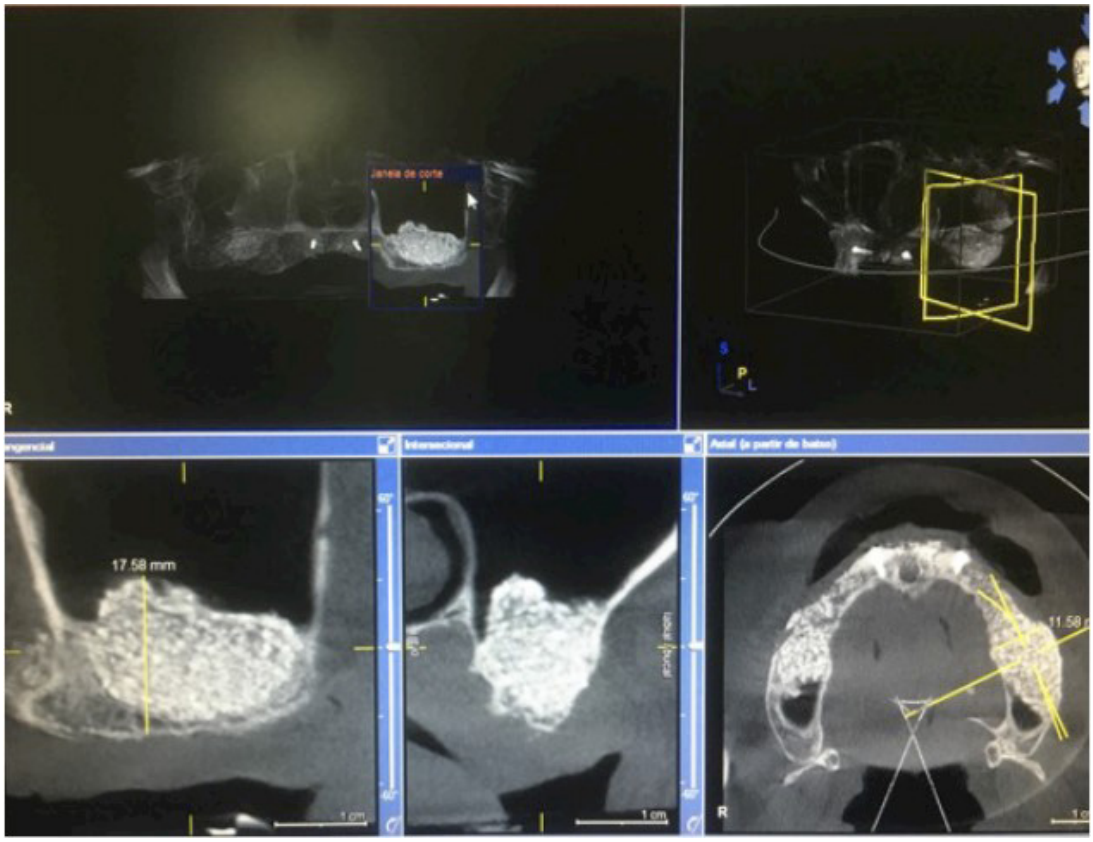

Figure 2. Tomographic aspect after 8 months of grafting procedures.

and absolute alcohol and diaphanized in xylol. After inclusion in paraffin, 5 µm thick longitudinal histological sections were obtained by a microtome (Leica RM 2125T, Nussloch, Germany). The slides were stained by the hematoxylin and eosin technique. Images of the histological sections were obtained by an optical microscope (Olympus BX41, Tokyo, Japan).

The histological analysis was performed in 3 sections of each sample, located in the peripheral and central portions of the cut. The histological sections were evaluated qualitatively and quantitatively. The qualitative analysis was based on the evaluation of the tissue components, including soft and mineralized tissues. Regarding soft tissues, the presence of inflammatory cells, areas of fibrosis, areas of necrosis and foreign body reactions were evaluated. On the mineralized tissues, the presence of biomaterial and mineralized tissue was evaluated. The quantitative analysis was performed using ImageJ software, which measured the total area of the cut, the area of biomaterial, the area of bone tissue and the area corresponding to soft tissues.

RESULT

In the qualitative histological analysis, histological sections revealed the presence of biomaterial surrounded by vital and immature bone tissue (Figure 3). Areas of mature bone were detected, but less frequently. No areas were found with soft tissue interposition between the surface of the biomaterial and the bone tissue. That is, direct contact of the bone tissue was observed on the surface of the biomaterial. Areas of biomaterial reabsorption were observed, characterized by the presence of multinucleated giant cells. Despite the presence of these cells, foreign body type reactions were not detected. Regarding soft tissues, no relevant changes were observed. In a general context, this tissue was presented with a moderate amount of collagen fibers, and focal areas with a number of collagen fibers were observed in some cuts. Inflammatory cells were detected in isolated foci, being predominantly monomorphonuclear, characterizing an inflammatory infiltrate of chronic nature. However, despite the discrete presence of these cells, the tissue did not have a relevant inflammatory process (Figure 3). Quantitatively, the histomorphometric analysis revealed different percentages of the soft and mineralized tissues of the grafted bed, being 28.8% of bone tissue, 27.4% of biomaterial and 43.6% of soft tissue.

DISCUSSION

Despite consensus in the literature that autogenous bone grafts are considered the gold standard because of their biological properties for the formation of bone tissue[6,7]. Biomaterials alternative to the use of autogenous bone graft, such as hydroxyapatite-based biphasic ceramics β-tricalcium phosphate has been shown to be effective for increasing bone availability, which allows implant installation and maintenance of prostheses with good predictability[10,14,15]. In fact, this study demonstrated that the use of biphasic ceramics based on hydroxyapatite and β-tricalcium phosphate used as a graft material in maxillary sinus surgeries promoted the formation of bone tissue in intimate contact with the remaining biomaterial particles which allowed the installation of the osseointegrated implant after 8 months of the surgical procedure of grafting.

The results of the histometric analysis of this study demonstrated that the biopsies removed from the maxillary sinuses previously grafted showed a percentage of bone tissue of 28.8% and presence of biomaterial remnants of 27.4%, and these results are in agreement with what was found in other studies. A clinical study comparing histologically and histomorphometrically the biphasic ceramic grafts with autogenous bone grafts in maxillary sinus lift surgeries found that the biopsies taken from the areas grafted with biphasic ceramic presented 28.2% of bone tissue and 32.9% of biomaterial after a waiting period between 6-8 months of the grafting procedure and implant installation, and that although the autogenous bone graft presented a greater amount of neoformed bone tissue (36.8%), this difference did not influence the clinical results of the implants installed in this study[8]. Another clinical study with a split-mouth model comparing grafted areas with biphasic ceramics based on hydroxyapatite and β-tricalcium phosphate with homogenous grafts in the maxillary sinus survey showed that the biopsies of the areas grafted with biphasic ceramic presented 24.0% of bone tissue and 25.4% of biomaterial remaining particles after a period

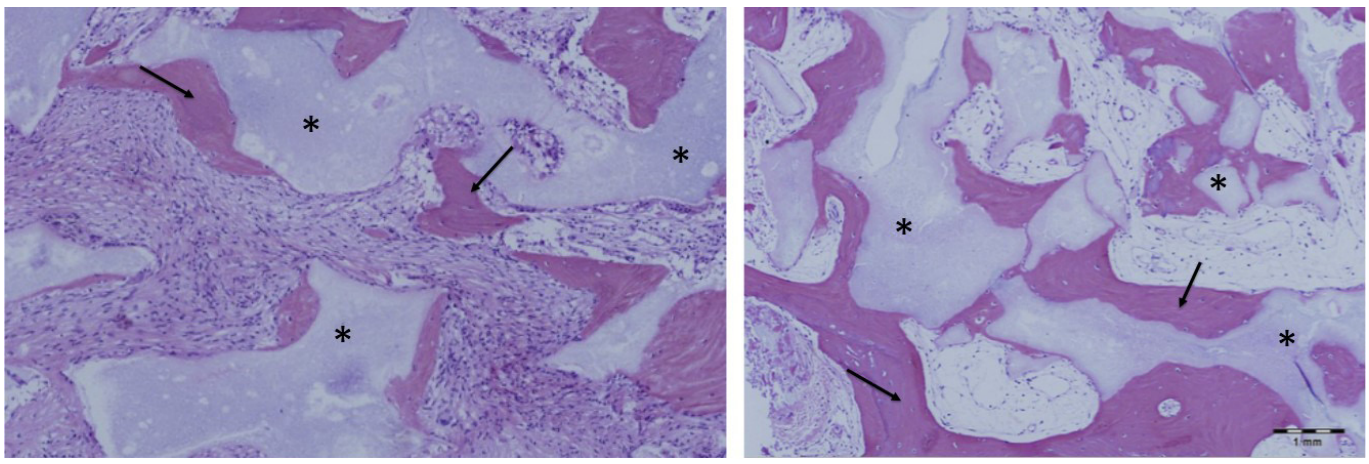

Figure 3. Vital and immature bone tissue after eight months of grafting procedures. Observe vital and immature bone tissue (asterisk) on the surface of the biomaterial (black arrow).

of 9 months after the grafting procedure and that the use of both grafts were efficient in obtaining sufficient bone availability for implantation of the implants[10].

It was observed in the histological description that the bone associated with the biomaterial particles were surrounded by vital bone, with the presence of few inflammatory cells that were associated with reabsorption gaps. To confirm that biphasic ceramics present a lower osteoconductive potential than other types of biomaterials such as xenogenic16 and homogenous[10]. These differences observed in the histological response do not influence the clinical properties of these different osteoconductive biomaterials in procedures of maxillary floor elevation[10,16]. However, the effect of different degrees of osteoconduction between biomaterials under less favorable guided bone regeneration clinical conditions is still uncertain.

Biphasic ceramics have been preferred in clinical use than the isolated use of hydroxyapatite and β-tricalcium phosphate since the association of these two products increased the potential for osteoconduction, bone formation and reduced reabsorptions of the biomaterial[13,14]. In fact, a pre-clinical study comparing bone repair in critical calvarial defects of rabbits grafted with biphasic ceramic based on hydroxyapatite and β-tricalcium phosphate compared to the isolated use of hydroxyapatite and β-tricalcium phosphate demonstrated that biphasic ceramics promoted a greater area of bone formation after 8 weeks of the surgical procedure (9.03 ± 3.39 mm2) compared to the other grafts (6.95 ± 3.51 mm2 and 4.04 ± 1.39 mm2, promoted by the of hydroxyapatite and β-tricalcium phosphate, respectively). The comparison of the histological composition between these different biomaterials and their results in the clinical results of the implants need to be investigated in the future.

The biphasic ceramic used in this study presents a proportion of 60% hydroxyapatite and 40% β-tricalcium phosphate, and it has been the one with the largest documentation in the literature[8,10,16]. However biphasic ceramics with different proportions than those used in this study have also been used. A preclinical study compared different proportions of biphasic ceramics in a model of critical defects in rabbit calvaria and that after 8 weeks biphasic ceramics with 60/40 and 20/80 ratio of hydroxyapatite and β-tricalcium phosphate showed similar amounts of (5.70 ± 1.28 mm2 vs. 5.20 ± 1.28 mm2) and the amount of new bone (7.29 ± 4.14 mm2 vs. 5.61 ± 1.28 mm2)[17]. A clinical study that evaluated the use of biphasic ceramic of the proportion of 30% hydroxyapatite and 70% β-tricalcium phosphate in procedures of maxillary floor elevation found a proportion of 29 ± 3% of bone tissue and of 26 ± 2% after 6 months of the procedure[15]. Another clinical study comparing the composition of the biopsies removed in maxillary sinus floor areas with biphasic ceramic in the proportion of 30% hydroxyapatite and 70% β-tricalcium phosphate showed that the biopsies presented a percentage of bone of 30.2% and percentage of remnant of biomaterial of 29.1%[18], and the results presented by these clinical studies are very similar to the findings of our study.

Despite the limitations of this study, such as the absence of a comparative control group, the low number of samples and the only execution of histological/histometric analysis, which confirmed the findings of other studies previously performed that the biphasic ceramic based on 60% hydroxyapatite and 40% β-tricalcium phosphate can be used in isolation in maxillary sinus lift procedures. The direct clinical comparison of this biomaterial with other ceramics and with other osteoconductive biomaterials should be performed in the future.

CONCLUSION

Based on the results obtained in this study, it was possible to conclude that biphasic ceramics based on hydroxyapatite and β-tricalcium phosphate showed a good osteoconductive behavior and allowed the installation of implants after maxillary sinus lift procedure. Also, it was possible the increase of the thickness of the floor of the maxillary sinus, being effective in the new bone formation. Also, it should be noted that no postoperative complications were observed with the use of this biomaterial.

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CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

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