Original Article

A Combination of Beta-tricalcium Phosphate, Plasmogel, and Platelet-rich Plasma Improves Long-term Bone Tissue Restoration after Complicated Lower Third Molar Surgery: A Nonrandomized Controlled Trial

Abstract

Background: A surgical removal of the lower third molars can lead to a number of complications, and bone restoration typically takes a large amount of time. The aim of the study was to investigate the effect of the combination of beta-tricalcium phosphate (β-TCP), plasmogel, and platelet-rich plasma on postsurgery bone tissue restoration by means of X-ray. **Subjects and Methods:** A total of 200 patients who underwent a complicated removal of the lower third molars were nonrandomly assigned to the experimental (EXP, n = 100) or control (CTR, n = 100) group. In the EXP group patients, sockets were filled with a combination of β-TCP, plasmogel, and platelet-rich plasma. In the CTR group, sockets were not treated. X-ray examinations were performed 3, 6, and 9 months (T1, T2, and T3) postsurgery to define bone quality on the Misch scale. The Mann–Whitney U-test was used for between-group comparison. **Results:** Aside from the overconsumption of sugars (more frequently in CTR) and marginally significant sex ratio difference (more females in CTR), the groups were equivalent. Although both groups improved on bone density with time, the EXP group demonstrated greater restoration at T1 ($U = 3431$, $P < 0.001$), T2 ($U = 3190$, $P < 0.001$), and T3 ($U = 3505$, $P < 0.001$) related to a greater percentage of D2 (dense thick porous cortical bone on the ridge and a coarse underlying trabecular bone). **Conclusion:** A combination of β-TCP, plasmogel, and platelet-rich plasma, compared to no treatment, facilitates bone tissue restoration after complicated surgical removal of the lower third molars.

Keywords: *Beta-tricalcium phosphate, bone tissue restoration, lower third molar removal, platelet-rich, plasma, X-ray*

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Introduction

The complicated third molar eruption is a widespread dental problem that is present in the vast majority of the general population and typically requires surgery.[1,2] The third molar extraction is a common and standard procedure.[1-5] Nevertheless, a tissue barrier that previously blocked the normal eruption of wisdom teeth prevents subsequent teeth removal and, thus, the removal of bone parts is required.[6] In the short term, teeth extraction may result in a number of postoperative complications such as swelling, pain, and trismus[4,5,7] or more serious as surgery site infection, dry socket,[4,7] or even medication-related osteonecrosis of the jaw.[8] In the long term, surgery drives a chain of complex cell development and migration processes that may lead to alveolar ridge bone resorption and apposition.[9,10]

A few materials were tested for bone tissue restoration facilitation, although the evidence for their effectiveness remains inconclusive.[5] Beta-tricalcium phosphate (β-TCP) is probably the most exhaustively investigated osteoplastic material. Compared to no-treatment, filling a socket with β-TCP reduces the alveolar ridge resorption rate at 3.5 months postsurgery[11] and increases bone density at 6 months postextraction with immediate implant insertion.[12] Combined with mineralized freeze-dried bone allograft, β-TCP also diminishes the percentage of poor (D4) bone quality at 2 months postsurgery, although a significant amount of graft remains in the socket.[13,14] Applied

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in combination with Type I collagen, β-TCP promotes some vital bone restoration.[15] Compared to freeze-dried bone allograft, β-TCP provides greater mineralization and the same level of alveolar ridge bone endurance.[16] In dynamics, β-TCP improves bone density (similarly to calcium phosphosilicate).[17]

However, compared to the autologous platelet-rich fibrin (PRF) plug, the β-TCP graft performs poorly on new bone formation.[18] Similarly, biphasic calcium phosphate, a composite of β-TCP and hydroxyapatite, supports new bone formation to the same degree as bovine xenograft[19] and to a lesser degree than the no-treatment condition.[20] To add, enrichment of the recombinant human bone morphogenetic protein-2 with β-TCP and hydroxyapatite particles does not improve alveolar ridge preservation.[21] Noteworthy, the majority of the mentioned studies restrained the observation period to 2–4 months; thus, the long-term osteoplastic effectiveness of the β-TCP is generally unknown.

Platelet concentrates may be beneficial for bone tissue restoration due to growth factors' effects.[22] Thus, a combination of the PRF and β-TCP is suggested to restore affected bones to a greater degree than each single compound alone. The addition of platelet-rich plasma (PRP) or platelet-derived growth factor to β-TCP leads to further improvement in bone quality and is related to a smaller amount of graft in the socket 2-month postextraction.[13,14] PRF seems to improve the alveolar ridge preservation and radiographic bone fill percentage.[9] Nevertheless, PRF application fails to significantly increase the region of newly formed bone[6] and only slightly impacts bone tissue density.[3] Regretfully, only one of the mentioned studies considered the bone restoration-promoting effects of the combination of β-TCP–PRP.

The aim of the present study was to estimate relatively long-term (up to 9-month postsurgery) effects of β-TCP–PRP combination on X-ray bone quality indicator in realistic clinical settings.

Subjects and Methods

A total of 200 consecutive patients (111 females and 89 males) participated in the study. The inclusion criteria were complicated lower third molar removal, age (18–85), and ability to give written informed consent. Pregnancy, infectious diseases, blood diseases, cancer, and adverse reactions to sodium heparin were noninclusion criteria. Patients were nonrandomly assigned either to the experimental (EXP) or to the control (CTR) group to either receive socket filling with an osteoplastic material, plasmogel, and platelet-rich plasma or recover bone tissue naturally under a blood clot, respectively. The demographic and clinical data on each group are summarized in Table 1. The study was conducted in accordance with the 2013 revision of the WHO declaration of Helsinki and was approved by the Local Ethical Review Board of the Kazakh Medical University of Continuous Education, Almaty, Kazakhstan issued on February 18, 2020 (protocol #2).

Table 1: Summary of demographic and clinical parameters of the participants

Parameter	EXP	CTR	χ^2	*P*
Sex ratio, female: male	49:51	62:38	3.4	0.064
Age, mean±SD	39.1±17.1	Not assessed	-	-
Ethnicity/race				
Kazakh/Asian	65	66	0.0	0.986
Russian/Caucasian	25	24		
Uyghur/Asian	10	10		
Family income				
Low	31	28	0.2	0.896
Middle	38	40		
High	31	32		
High sugar consumption (daily)	56	74	7.1	0.008
Family history of lower third molar abnormality	65	54	2.5	0.113
Tooth position				
Lingual inclined	16	13	3.7	0.599
Buccolateral inclined	16	13		
Mediolateral inclined	17	13		
Distolateral inclined	16	14		
Vertical	17	27		
Horizontal	18	20		

EXP: Experimental group; CTR: Control group; SD: Standard deviation

After signing the informed consent form, the participants entered a maxillofacial department of a clinical hospital, provided their demographical data, and underwent clinical and radiological examinations. On the following day, surgical removal of the lower third molars was performed. The surgery followed the standard technique assuming cutting out an angled mucoperiosteal flap. The extraction of a tooth was carried out by an atypical method, in some patients the tooth was fragmented to preserve the surrounding bone tissue. In CTR patients, the operation ended with the formation of a blood clot and the sewing of the wound.

In EXP patients, after the tooth extraction, 9 ml of venous blood was sampled with a butterfly needle and vacuum blood collection tubes. The samples were centrifuged for 4 min at 3200 rotations/min to split the plasma enriched with platelet factors from an erythrocyte-leukocyte clot. Following that, 0.5–1 ml of the plasma was injected along the transitional fold at the level of the socket. The remainder of the plasma was exposed to 80°C temperature for 4 min to obtain a plasmogel. The plasmogel mixed with a β-TCP (Sorbonne, South Korea) in a 1:3 ratio was placed in the bone cavity, and sutures were applied to a mucous membrane. X-ray examinations (orthopantomography and three-dimensional [3D] computed tomography [CT]) were performed with a cone-beam CT device using Ez3D-i (Vatech, Republic of Korea) software at 3, 6, and

9 months postsurgery. Bone tissue quality was assessed using the Misch scale.

Group equivalence on demographic and clinical data at baseline was assessed with the Chi-square test. Temporal dynamics of bone quality on the Misch scale were evaluated with Friedman's ANOVA with a posteriori Wilcoxon's *W*-tests featuring Bonferroni correction for a number of time points. Last, between-group differences at each time point were estimated by means of Mann–Whitney's *U*-test. Statistical processing was performed using the IBM SPSS 21.0 software (IBM, Armonk, NY, USA).

Results

EXP and CTR groups did not differ in terms of ethnic/racial composition, family income, or third lower molar position [all $P > 0.1$, Table 1]. However, the EXP group featured a trend to a greater percent of male patients and a significantly smaller percent of patients who reported daily consumption of sugars.

While comparing different time points within-group, a significant effect of a time point occurs: in the CTR group, mean ranks R3 = 1.9, R6 = 2.0, R9 = 2.2, S (2, 297) = 7.4, $P = 0.025$; in the EXP group, mean ranks R3 = 1.9, R6 = 2.0, R9 = 2.1, S (2, 297) =7.5, $P = 0.023$. A posteriori Wilcoxon tests in the CTR group revealed significant improvement between the T2 and T3 (W[198] =2.6, $P = 0.011$, corrected $P = 0.032$), and T1 and T3 (W[198] =2.6, $P = 0.010$, corrected $P = 0.029$), although no difference between the T1 and T2 (W[198] =0.1, $P = 0.908$). In the EXP group, significant improvement occurred only between the T1 and T3 (W[198] =2.6, $P = 0.009$, corrected $P = 0.027$), not in T1-T2 (W[198] =2.0, $P = 0.041$, corrected $P = 0.124$) and T2-T3 pairs (W[198] =1.0, $P = 0.317$).

Between-group differences demonstrated more improvement in bone density in the EXP group compared to the CTR group at each time point [Table 2]. Thus, patients from both groups gradually improved, although the EXP group participants feature greater bone density (greater incidence of D2) at each measurement.

Table 2: Between-group comparison of the densitometry score

Time point	Quality score	EXP	CTR	*U*	*P*
3-month	D5	7	4	3431	<0.001
	D4	3	9		
	D3	12	43		
	D2	73	42		
	D1	5	2		
	Mean rank	85	116		
6-month	D5	3	10	3190	<0.001
	D4	2	10		
	D3	4	26		
	D2	88	52		
	D1	3	2		
	Mean rank	82	119		
9-month	D5	1	4	3505	<0.001
	D4	2	2		
	D3	0	29		
	D2	96	63		
	D1	1	2		
	Mean rank	86	115		

EXP: Experimental group; CTR: Control group; *U*: Mann–Whitney test value

Discussion

The principal aim of the study was to estimate the effects of a combined β-TCP–PRP-plasmogel filling on the long-term dynamics of bone quality of an alveolar ridge damaged during an atypical surgical removal of the lower third molars. β-TCP application is considered the main factor of bone tissue restoration; however, an addition of a PRP and plasmogel, aside from preventing postsurgical complications, was also considered an improvement-facilitating factor. Consistent with our hypothesis, the EXP group patients demonstrated greater rates of achieving the D2 that corresponds to a dense thick porous cortical bone on the ridge and a coarse underlying trabecular bone. Although both EXP and CTR groups improved on bone tissue density with time, patients of the EXP group generally improved faster, and to the end point of follow-up (9 months posttreatment), 96% of the EXP patients (vs. 63% of CTR patients) reached the D2.

Compared with 2-month postsurgery data of patients in Ntounis *et al*.'s study,[14] patients in the current study improved in the bone quality to a greater degree to the 3-month point. A total of 55% first (CTR) group of Ntounis *et al*.'s study[14] featured D4 and 33% featured D2 + D3, while 13%, 43%, and 42% of our CTR participants presented D4 + D5, D3, and D2, respectively. The third group of Ntounis *et al*.'s study[14] demonstrated 42% and 58% ratios for D2 and D3, respectively, while our EXP group featured ratios of 73% and 12% for D2 and D3, respectively. There are a number of possible reasons for these discrepancies; however, we believe that the results mismatch is at least partially accounted for by the time interval between surgery and measurement (3 months in our study vs. 2 months in Ntounis *et al*.'s study[14]). Thus, our results corroborate the β-TCP–PRP role in improving bone quality using relatively large samples and, more importantly, show that benefits from the β-TCP–PRP application persist at least up to 9 months postsurgery.

Although the only alveolar ridge preservation measure in our study was bone quality, we believe that our results are in line with those of preceding studies suggesting treatment-related improvement in bone density[12,17] and alveolar ridge endurance.[11,16] Nevertheless, the scale used in our study cannot distinguish between new-grown bone and graft remains β-TCP and its combinations are notorious.[13] Thus, we cannot contribute to current literature generally suggesting slower new bone formation in β-TCP-treated patients.[18,20]

The most important limitation of the study is the choice of a no-treatment CTR group, which does not allow to differentiate between the placebo effects, specific effects of β-TCP and PRP, and putative specific effects of a plasmogel. This gap is partly covered by data of Ntounis *et al*.[14] who demonstrated a significant improvement in bone quality dynamics with the addition of PRP. Some studies on PRF sharing the action mechanism with PRP also suggest specific PRF-related bone tissue improvement[9] and, more importantly, reducing residual graft amount.[13,14] The second limitation is a nonrandom approach to group allocation that could introduce a bias related to baseline intergroup differences. Indeed, a trend was demonstrated to intergroup differences in male/female ratio and in sugar consumption habits. Note that the sex ratio difference does not explain bone quality differences. Females generally feature greater regions of osteogenesis after the third molar extraction, compared to males.[6] A smaller percent of the EXP group participants were female; nevertheless, this group improved greater in terms of bone quality. Sugar excessive consumption could influence oral microbiota, although this influence is not likely to cause highly significant intergroup bone quality differences revealed in the current study. However, one cannot be sure that the groups were equivalent on any important factor. Keeping in mind these limitations, the results should be treated with caution.

Conclusion

A combination of the β-TCP, PRP, and plasmogel provides more rapid bone tissue restoration after the lower third molar removal, compared to no treatment. Greater bone quality in the β-TCP-PRP-plasmogel group is evident at 3-, 6-, and 9-month post-surgery. Thus, the aforementioned combination is beneficial as a mean for a bone tissue repair facilitation.

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Conflicts of interest

There are no conflicts of interest.

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