

Evaluation of the Efficacy of Metformin Topical Application on Bone Healing Around Immediate Dental Implants (Radiographic Study)

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Abstract

Background: Early implant fixation may reduce the length of treatment and can assist in preserving the peri-implant tissue envelope, but the healing of the residual socket gap is unpredictable in low-density posterior maxillary bone. Guided bone regeneration (GBR) enhances the local healing condition, and the simplest osteogenic and angiogenic adjunct proposed is topical metformin.

Purpose: To determine, using a standardized radiographic follow-up, the effect of locally delivered 1% metformin gel in enhancing bone healing surrounding immediately placed dental implants augmented with GBR.

Materials and Methods: Twelve medically free female patients requiring extraction and immediate implant placement in the posterior maxilla were randomly assigned to a study group treated with 1% metformin gel plus GBR or to a control group treated with GBR alone. Crestal bone level and CBCT-derived peri-implant radiographic density were assessed at baseline, 6 months, and during the extended 12-month follow-up analysis.

Results: Crestal bone level showed no significant difference between the metformin and control groups at 6 months or at the 12-month assessment ($p = 0.522$ and $p = 0.485$, respectively). At 12 months, the mean crestal bone level was 1.43 ± 0.60 mm in the study group and 1.84 ± 0.97 mm in the control group. CBCT-derived peri-implant radiographic density was significantly higher in the study group at 6 months ($p = 0.015$) and remained significantly higher at 12 months (1175.83 ± 758.40 versus 484.67 ± 285.10 , expressed as software-generated gray-scale values; $p = 0.008$). Within the study group, radiographic density increased significantly from baseline to 12 months ($p = 0.021$), whereas the control group did not show a significant change ($p = 0.081$).

Conclusion: Within the limitations of this small randomized radiographic study, topical 1% metformin gel used as an adjunct to GBR during immediate implant placement was associated with a sustained increase in CBCT-derived peri-implant radiographic density up to 12 months, without evidence of an unfavorable effect on marginal bone stability.

Keywords: Metformin; immediate implant placement; guided bone regeneration; osseointegration; CBCT; radiographic density; crestal bone level; posterior maxilla.

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Introduction

Dental implants are now a routine treatment option for replacing missing teeth because they restore masticatory function, preserve adjacent tooth structure, and provide favorable long-term survival when case selection and surgical execution are appropriate ^(1,2). After extraction, however, the alveolar ridge does not remain static. The socket undergoes dimensional remodeling, and this remodeling may affect implant position, emergence profile, soft-tissue contour, and the need for additional augmentation ⁽³⁻⁵⁾.

Immediate implant positioning was also proposed to minimize the amount of surgeries and the overall course of

treatment. It can also be used to preserve the peri-implant tissue architecture when carried out in an appropriate socket. The method is more challenging in the posterior maxilla, where the extraction socket can be broader than the implant diameter and the native bone is generally less dense than elsewhere. These characteristics may complicate primary stability, gap management, and positioning in the form of a prosthesis (5-11).

The distance between the implant and socket wall which is often referred to as the horizontal gap in implant therapy or the jumping distance is a major biological concern in immediate implant therapy. Small fissures with intact

socket walls can be healed with minimal intervention, whereas larger fissures, thin buccal plates, and the lack of low-density bone make the spontaneous bone fill predictability less predictable. This is why GBR that includes particulate grafts and resorbable membranes have been regularly applied to aid in space maintenance, osteoconduction, and inhibition of soft-tissue infiltration during bone repair (7-10,12-14).

Even though GBR offers a favorable scaffold to regeneration, biologically active agent can be added to increase cellular processes that lead to initial osteogenesis, angiogenesis, and mineralization. Metformin, a commonly used biguanide medication in type 2 diabetes mellitus, has gained interest in bone-regeneration studies since it is able to activate AMP-activated protein kinase, enhance osteoblastic differentiation, lessen oxidative stress, and affect angiogenic signaling. The local delivery method is clinically favorable since it has the capability of localizing the drug to the area of surgery and minimally dispersing throughout the body (15-26).

The current randomized radiographic trial was thus intended to determine whether topical 1% metformin gel combined with GBR leads to a future enhancement in peri-implant bone healing in the case of immediate placed implants in the posterior maxilla. To investigate the potential to continue the early radiographic density response detected as a result of the process of osseointegration post-prosthetic rehabilitation and functional loading, the extended 12-month analysis was introduced (15-18,27,28).

Materials and Methods

Study design and setting

It was a parallel-arm randomized controlled radiography study in the outpatient clinic of the Oral and Maxillofacial Surgery Department, Faculty of Dental Medicine, Assiut Branch, Al-Azhar University, Egypt. The paper was written to provide the clinical intervention and radiographic results in a clear and repeatable way.

Ethical approval and consent

The Ethical Committee of the Faculty of Dental Medicine, Al-Azhar University gave its approval to the study protocol (approval no. AUAREC2022011-5). All the participants were given a clear explanation of the surgical procedures, anticipated benefits, potential risks, follow-up, and data use. Informed consent was taken in written form prior to the enrollment and patient confidentiality was ensured during the study.

Participants

There were twelve women patients aged 18-45 years. All the patients needed to have hopeless maxillary posterior teeth extracted or retained roots extracted and immediately implanted. To qualify, there was to be medical fitness based on the modified Cornell Medical Index (29), adequate residual bone size to permit the implantation of at least 10 mm in length, a clinically healthy recipient site, and acceptable oral hygiene.

Exclusion criteria

Patients were not included in case they had uncontrolled systemic disease that may have influenced bone healing,

active pathology at the implantation site, heavy smoking, alcohol or drug abuse, para functional habits, metabolic bone disease, history of chemotherapy or radiotherapy, or current or past use of medication that may have interfered with bone turnover.

Randomization, allocation concealment, and blinding

A randomization sequence was generated using a computer and the participants were randomly assigned in a 1:1 ratio to two equal groups (n = 6 per group). The study population was subjected to immediate implantation with the topical application of 1% metformin gel in combination with guided bone regeneration compared to the control group where the population received the same immediate implantation and guided bone regeneration protocol, but was not subjected to metformin.

The operating surgeon could not be blinded as the surgeon needed to apply the metformin gel in the placement of the implants. All CBCT pictures were anonymized and coded to reduce the chances of assessment bias during radiographic analysis. An examiner who was not aware of the treatment allocation measured crestal bone level and CBCT-based peri-implant radiographic density measurements. The group codes were revealed after the radiographic measurements and statistical analysis were complete.

Preparation of 1% metformin gel

Gellan gum was used in preparing the metformin gel. Gellan gum (0.4%) was moistened in distilled water at 95 C. Mannitol, metformin hydrochloride, citric acid, methylparaben and propylparaben were then added to the mixture which was then stirred, constantly. Ionic gelation by the addition of sodium citrate (0.5%) was followed and the end product was prepared to about 1% metformin and cooled followed by formation of the gel (30).

Surgical protocol

All surgical interventions were done under local anesthesia following normal antiseptic preparation. The specified tooth or retained root has been extracted in an traumatic manner, whereas the socket was meticulously debrided. Sequential osteotomy preparation was done with abundant irrigations. Apical engagement of implants in a prosthetically guided position was used to achieve primary stability. The implant surface of the study group was coated with 1% metformin gel right before placing the implant. In both groups, the residual peri-implant gap was filled with alloplastic bone graft and covered with a resorbable collagen membrane. The main soft-tissue closure was done by resorbable sutures.

Postoperative care and prosthetic phase

Postoperative prescriptions were amoxicillin/clavulanic acid 1 g twice a day in 7 days, ibuprofen 600 mg on-demand analgesic and 0.12% chlorhexidine mouthwash 7 days. Removal of sutures was done after about two weeks. Second-stage surgery followed 6 months with exposure of implants and placement of the healing-abutment, and final prosthetic rehabilitation.

Outcome variables

The change in peri-implant radiographic density as assessed by CBCT in the form of software-generated gray-

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scale values was the primary radiographic outcome. The measurements were made in standardized comparisons among the groups and across the periods of follow up and were not considered to be absolute bone mineral density or actual medical CT Hounsfield units. The second radiographic outcome was crestal bone level.

Peri-implant radiographic density was measured with an implant-length-adjusted rectangular region of interest (ROI). The coronal and apical limits of the ROI were situated 1 mm away along the coronal and apical ends of the implant respectively. The longitudinal dimension of the ROI was varied as well due to the difference in the lengths of the implants. The ROI was aligned such that, the surrounding peri-implant bone occupied about two thirds of the ROI with only a third of the bone occupying the body of the implant. The ROI dimensions, orientation and relative position of each implant were replicated at baseline and at the 6- and 12-month assessments using the implant platform, apex and long axis as fixed reference points. The average gray-scale value in the ROI produced by the software was documented to analyse.

Sample size and power considerations

This study was undertaken as a pilot randomized controlled trial because no reliable preliminary dataset was available that fully matched the present protocol, including immediate implant placement, guided bone regeneration, local application of 1% metformin gel, and CBCT assessment over a 12-month follow-up period. The pilot sample therefore included 12 participants, who were allocated equally between the two treatment groups.

An exploratory sample-size projection was conducted to inform the design of a follow-up definitive trial by using CBCT-measured peri-implant radiographic density at 12 months as the key radiographic outcome. Mean radiographic density at this time was 1175.83 ± 758.40 in the metformin group and 484.67 ± 285.10 in the control group. The pooled standard deviation generated by these values was 572.91 and the small-sample-corrected standardized effect size was Hedges' $g = 1.11$. The estimated minimum sample size was 14 participants per group with a two-sided level of significance of 0.05, statistical power of 80%, and equal distribution of participants between the groups. Once the potential 10% loss to follow-up is considered, the suggested number of participants would be 16 participants per group, which would make it 32 participants in total. Since this estimation was based on pilot data, the results of the present research are to be viewed as preliminary and the estimated sample can be considered as the minimum to conduct a confirmative study in the future.

Statistical analysis

Continuous variables were summarized as mean $\pm$ standard deviation and, when appropriate, median and range. Intergroup comparisons were performed using independent-samples t-tests or Mann-Whitney U tests according to data distribution. Intragroup changes were analyzed using paired t-tests or Wilcoxon signed-rank tests. Statistical significance was set at $p < 0.05$. Effect

sizes were also reported to support interpretation because of the limited sample size.

Results

Participant characteristics and follow-up

Twelve patients were enrolled and allocated equally to the metformin and control groups. The mean age was 30.83 ± 10.23 years in the study group and 36.67 ± 8.09 years in the control group, with no statistically significant difference between groups ($p = 0.299$). Healing was uneventful in both groups, and no early implant loss was recorded during the evaluated follow-up period.

Participant progression through enrollment, allocation, follow-up, and analysis is shown in Figure 1. Twelve eligible participants entered the trial and were randomly allocated in equal numbers to the metformin and control groups ($n = 6$ per group). All 12 randomized participants received their assigned intervention and were included in the radiographic analyses reported at baseline, 6 months, and 12 months, with no post-randomization exclusions.

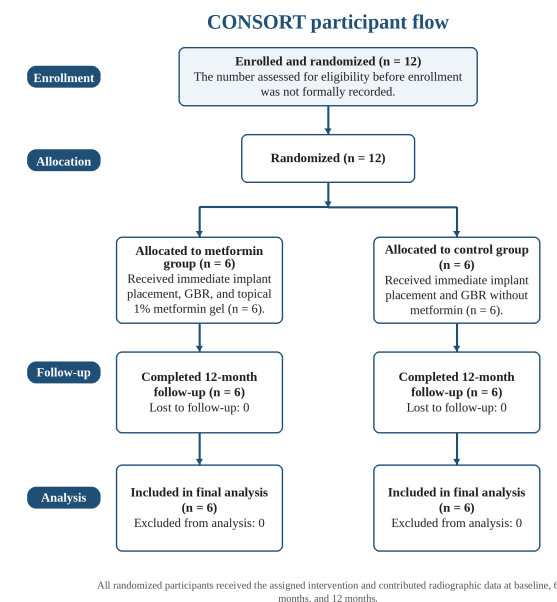


Figure 1. CONSORT flow diagram showing participant allocation, follow-up, and analysis through 12 months.

Crestal bone level

At baseline, the mean crestal bone level was 1.97 ± 0.88 mm in the study group and 2.46 ± 1.07 mm in the control group ($p = 0.337$). The values at 6 months were 1.53 ± 0.62 mm and 1.87 ± 0.98 mm respectively, and there is no statistically significant intergroup difference ($p = 0.522$). The within-group change from baseline to 6 months was statistically significant in the study group ($p = 0.046$), but not in the control group ($p = 0.068$). At the extended 12-month evaluation, the study group had numerically lower values of crestal bone level than control (1.43 ± 0.60 mm versus 1.84 ± 0.97 mm) but the difference between them was not significant ($p = 0.485$). Between baseline and 12 months, the two groups had significant within-group improvement ($p = 0.046$ in the study group and $p = 0.028$ in the control group), which indicates that the marginal bone level stabilized at the follow-up.

Table 1. Comparison of crestal bone level between groups at baseline, 6 months, and the extended 12-month follow-up.

Crestal bone variable	Study group	Control group	p value	Effect size
Baseline, mean $\pm$ SD (mm)	1.97 $\pm$ 0.88	2.46 $\pm$ 1.07	0.337	0.068
Baseline, median (range)	1.8 (1.0-3.1)	2.1 (1.5-4.1)		
6 months, mean $\pm$ SD (mm)	1.53 $\pm$ 0.62	1.87 $\pm$ 0.98	0.522	0.052
6 months, median (range)	1.4 (0.8-2.4)	1.6 (0.8-3.6)		
12 months, mean $\pm$ SD (mm)	1.43 $\pm$ 0.60	1.84 $\pm$ 0.97	0.485	0.278
12 months, median (range)	1.29 (0.72-2.31)	1.59 (0.81-3.55)		
Within-group p value (baseline to 6 months)	0.046*	0.068		
Within-group effect size (baseline to 6 months)	0.676	0.515		
Within-group p value (baseline to 12 months)	0.046*	0.028*		
Within-group effect size (baseline to 12 months)	0.770	0.856		

SD = standard deviation; * statistically significant at $p < 0.05$. Intergroup comparisons were performed using

Mann-Whitney U tests; within-group comparisons were performed using Wilcoxon signed-rank tests versus baseline. The 12-month crestal bone level values should be confirmed by the final standardized follow-up radiographs before publication if these data are still provisional.

Figure 2. Box-plot distribution of crestal bone level in the study and control groups at baseline, 6 months, and 12 months.

Figure 3. Mean $\pm$ SD crestal bone level changes in the study and control groups at baseline, 6 months, and 12 months.

(a)

(b)

(c)

Figure 4. Representative CBCT image showing the crestal bone-implant relation in a control-group case: (a) immediate postoperative view, (b) 6-month follow-up, and (c) 12-month follow-up.

(a)

(b)

(c)

Figure 5. Representative CBCT image showing the crestal bone-implant relation in a study-group case: (a) immediate postoperative view, (b) 6-month follow-up, and (c) 12-month follow-up.

CBCT-derived peri-implant radiographic density at 6 and 12 months

Baseline CBCT-derived peri-implant radiographic density was numerically higher in the study group than in the control group, but the difference was not statistically significant (986.74 $\pm$ 768.27 versus 564.67 $\pm$ 352.42; $p = 0.310$). At 6 months, radiographic density increased in the study group and decreased slightly in the control group, resulting in a statistically significant intergroup difference (1124.88 $\pm$ 761.59 versus 489.17 $\pm$ 323.32; $p = 0.015$). At the 12-month assessment, the study group continued to show higher CBCT-derived peri-implant radiographic density than the control group (1175.83 $\pm$ 758.40 versus 484.67 $\pm$ 285.10; $p = 0.008$). The within-group increase from baseline to 12 months was significant in the study group ($p = 0.021$), whereas the control group did not demonstrate a significant change ($p = 0.081$). The intergroup effect size at 12 months was large (0.902), supporting the radiographic relevance of the density difference despite the small sample size.

Table 2. Comparison of CBCT-derived peri-implant radiographic density between groups at baseline, 6 months, and the extended 12-month follow-up.

Peri-implant radiographic density variable	Study group	Control group	p value	Effect size
Baseline, mean $\pm$ SD	986.74 $\pm$ 768.27	564.67 $\pm$ 352.42	0.310	0.389
Baseline, median (range)	817.2 (192.3-2446.5)	584.5 (107.0-938.0)		
6 months, mean $\pm$ SD	1124.88 $\pm$ 761.59	489.17 $\pm$ 323.32	0.015*	0.833

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6 months, median (range)	950.2 (341.4- 2587.7)	460.0 (187.0- 823.0)		
12 months, mean +/- SD	1175.83 +/- 758.40	484.67 +/- 285.10	0.008*	0.902
12 months, median (range)	992.0 (395.0- 2655.0)	459.0 (175.0- 825.0)		
Within-group p value (baseline to 6 months)	0.028*	0.094		
Within-group effect size (baseline to 6 months)	0.858	0.684		
Within-group p value (baseline to 12 months)	0.021*	0.081		
Within-group effect size (baseline to 12 months)	0.872	0.655		

SD = standard deviation; * statistically significant at $p < 0.05$. Intergroup comparisons were performed using Mann-Whitney U tests; within-group comparisons were performed using Wilcoxon signed-rank tests versus baseline. The 12-month radiographic density values should be confirmed by the final standardized follow-up radiographs before publication if these data are still provisional. Values represent software-generated CBCT gray-scale measurements and should not be interpreted as absolute Hounsfield units.

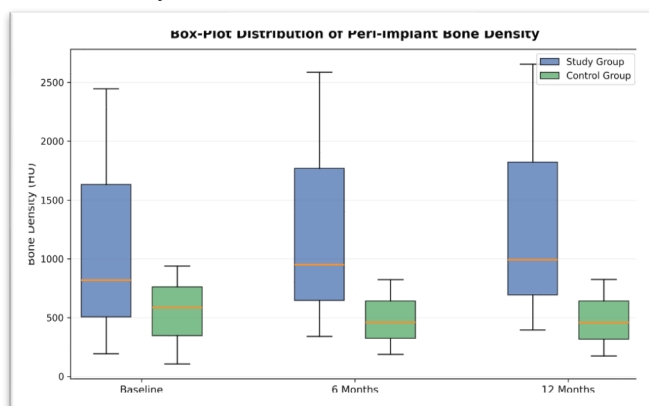


Figure 6. Box-plot distribution of CBCT-derived peri-implant radiographic density in the study and control groups at baseline, 6 months, and 12 months.

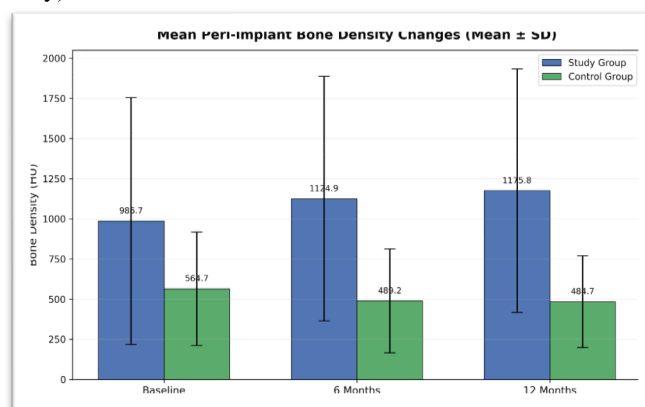


Figure 7. Mean +/- SD CBCT-derived peri-implant radiographic density changes in the study and control groups at baseline, 6 months, and 12 months.

(a) (b) (c)

Figure 8. Representative CBCT radiographic-density measurement at the 12-month follow-up in a control-group case: (a) immediate postoperative view, (b) 6-month follow-up, and (c) 12-month follow-up. The annotated region of interest illustrates the software-based peri-implant radiographic-density assessment.

(a) (b) (c)

Figure 9. Representative CBCT radiographic-density measurement at the 12-month follow-up in a study-group case: (a) immediate postoperative view, (b) 6-month follow-up, and (c) 12-month follow-up. The annotated region of interest illustrates the software-based peri-implant radiographic-density assessment.

Discussion

This randomized radiographic study examined whether topical 1% metformin gel could add a measurable regenerative benefit when used with GBR around immediately placed implants in the posterior maxilla. The rationale for using metformin was based on its reported osteogenic, angiogenic, antioxidant, and anti-inflammatory effects, which may enhance osteoblastic differentiation, mineralized matrix formation, and peri-implant bone maturation when delivered locally at the surgical site (15,19,22,23).

Placing immediate implants in posterior maxilla is a clinically difficult scenario due to the fact that the area is usually low in bone density, cancellous bone structure, and there is often a mismatch between the site of extraction and the size of the implant. This can produce a residual peri-implant gap which can influence clot stability and bone fill unless adequately addressed. Past research has stressed that predictable short-term implant outcomes relied on cautious case selection, sufficient primary stability, intact socket walls, proper positioning of the implant, and appropriate management of the peri-implant defect (5,7,9,11).

In the above study, all the patients included were females. This must be taken into account during the interpretation of the results as sex-related biological factors and hormonal effects could influence bone remodelling, bone turnover

and response to healing. The role of estrogen in bone homeostasis is significant: it controls the activity of osteoblast and osteoclast, thus, a female-only sample can demonstrate a particular trend of bone reaction (31). This could have minimized sex-related differences between the two groups but it also constrained the generalizability of the results to male patients.

The 6-month follow-up was prolonged to 12 months to establish whether the radiographic changes that were seen in the early stages of the process of osseointegration could be sustained following the rehabilitation and functional loading of the prosthetic. This mattered since peri-implant bone post-loading is still in the process of remodelling, and the early increase in radiographic-density may not always be maintained in the long term. Previous literature on implants has pointed out the significance of primary stability, control of micromotion, and transition to secondary biological stability (27,28).

In terms of crestal bone level, the study group had a mean of 1.97 ± 0.88 mm at baseline, which dropped to 1.53 ± 0.62 mm at 6 months and 1.43 ± 0.60 mm at 12 months. In the control group, the mean value decreased from 2.46 ± 1.07 mm at baseline to 1.87 ± 0.98 mm at 6 months and 1.84 ± 0.97 mm at 12 months. The results of these findings suggest that the marginal bone behavior of the two groups is stable and this could be attributed to atraumatic extraction, correct positioning of implants and the use of GBR. This is consistent with those before it who have reported that grafting and membrane coverage are beneficial to keeping the peri-implant defect space and improving bone regeneration in the immediate placed implant area (10,13,14).

There was also no statistically significant difference in intergroup comparison of crestal bone level at baseline, 6 months and 12 months in the study and control groups. Nevertheless, the study group had numerically lower values of crestal bone level values during the follow-up period. This could reflect a positive response to the use of metformin but again the small size of the sample and the multifactoriality of the marginal bone remodeling process could have prevented the statistical significance of the difference.

Regarding CBCT-derived peri-implant radiographic density, the study group showed a baseline mean value of 986.74 ± 768.27 , which increased to 1124.88 ± 761.59 at 6 months and 1175.83 ± 758.40 at 12 months. This significant increase suggests that topical metformin may have enhanced bone maturation and mineralization around the implants. These findings are supported by Marycz et al., who reported that metformin enhanced osteogenic differentiation and increased bone density, and by Fang et al., who demonstrated improved alveolar bone regeneration using metformin-incorporated scaffolds (15,22). Serrão et al. also reported improved peri-implant bone healing with metformin in an experimental model (23).

In the control group, radiographic density decreased slightly from 564.67 ± 352.42 at baseline to 489.17 ± 323.32 at 6 months and 484.67 ± 285.10 at 12 months, without a statistically significant intragroup change. This

suggests that GBR alone may have maintained the peri-implant healing environment but did not produce a marked radiographic density increase. Therefore, the additional improvement observed in the study group may reflect the biological effect of metformin beyond the scaffold effect of GBR.

Intergroup comparison showed no statistically significant difference in radiographic density at baseline, while the study group demonstrated significantly higher values than the control group at both 6 and 12 months. This indicates that the effect of metformin was maintained beyond the early healing phase and after loading. These results are in agreement with Krishnakumar et al., who reported improved peri-implant bone parameters after local application of 1% metformin gel, and with Pradeep et al., who found favorable clinical and radiographic outcomes following the use of 1% metformin gel in periodontal intrabony defects (16,17). Moreover, Patel et al. concluded that metformin may have promising effects on implant bioactivity and osseointegration, although further clinical evidence is still required (18).

The difference between crestal bone level and radiographic-density outcomes may be explained by the nature of each parameter. Crestal bone level mainly reflects marginal bone position and is influenced by surgical, prosthetic, and biological factors. In contrast, CBCT-derived peri-implant radiographic density may be more sensitive to changes in mineralization and maturation of newly formed peri-implant bone. Therefore, the main detectable effect of metformin in the present study appeared to be improvement in peri-implant radiographic density rather than a statistically significant change in marginal bone level.

Topical 1% metformin gel could be regarded as a promising addition to GBR in the context of the immediate placement of implants in the posterior maxilla with the limitations of this paper. The limited sample size, the female-only sample and shortcomings of CBCT-based radiographic density measurements must be factored in, though. It is suggested that further randomized clinical trials, that involve sexes, larger sample sizes, standardized radiographic regimes, and extended follow-ups should be conducted.

Clinical implications

Clinically, topical 1% metformin gel could prove to be an effective adjunct to GBR when immediate implant placement is being undertaken particularly in the posterior maxillary region that has less bone density. The method is cheap, straightforward and biologically plausible. But existing evidence must be considered as provisional. Introducing metformin as an alternative to good surgical principles, primary stability, atraumatic extraction, proper positioning of three-dimensional implants, and good GBR technique would be unacceptable.

The most feasible consequence of this research is that a local bioactive adjunct can enhance the radiographic-density response surrounding immediately placed implants, in case it is incorporated in a standard graft-and-membrane regimen. This could be helpful in clinical

practice where the surgeon is worried about delayed bone maturation or low-density posterior maxillary bone.

Limitations

There are a number of limitations to note. The sample was small, and all women were involved which restricts generalizability. Though ROI position was normalized over the total implant during all the assessment periods, about one third of the chosen region was within the implant body; the measured gray-scale values could have thus been partially due to metal-related artifacts. These values were not considered to be absolute bone mineral density or actual medical CT Hounsfield units but interpreted as the relative CBCT-derived peri-implant radiographic density values. Scanner settings, field of view and ROI selection and software workflow can also influence measurements. The other limitation is that the 12-month radiographic examination should be interpreted cautiously when some values have not yet been finalized through standardized radiographic verification. Moreover, the research lacked histologic examination, bone turnover biochemical markers, and larger multicenter sample. These problems reduce the possibilities of clarifying the cellular mechanism that exactly happens to explain the radiographic density improvement.

Recommendations for future research

Future randomized trials ought to involve bigger and more varied cohorts of patients, extended follow-up intervals, unified loading guidelines in relation to prosthetics, and automatic acquisition of CBCT parameters. Comparisons of various concentrations of metformin, delivery vehicles and combinations with platelet concentrates or growth-factor based strategies would also be useful. A more comprehensive view of the clinical value of topical metformin in implant dentistry would be offered by studies that integrate radiographic findings with the parameters of implant stability, clinical peri-implant parameters, and patient-reported results.

Conclusion

Within the limitations of this small randomized radiographic trial, topical 1% metformin gel used with GBR during immediate implant placement was linked to a significant and sustained increase in CBCT-based peri-implant radiographic density. Crestal bone level remained stable in both groups, with no significant intergroup difference. These findings should be validated by larger long-term randomized studies to determine the optimal dose and carrier system and the clinical indications for local use of metformin in implant dentistry.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Ethical Committee of the Faculty of Dental Medicine, Al-Azhar University (approval no. AUAREC2022011-5). Written informed consent was obtained from all participants.

Conflict of interest

The authors declare no conflict of interest related to this study.

Funding

No external funding was declared.

Data availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request, subject to institutional and ethical restrictions.

Author contributions

Kreman Mohamed Ebeid Mohamed: conceptualization, methodology, patient selection, surgical procedures, data collection, radiographic analysis, statistical analysis, and original draft preparation. Mohamed Mahgob Al-Ashmawy: supervision, study design, validation, scientific revision, and final approval. Ahmed Mohamed Ismail: clinical supervision, methodological guidance, data interpretation, manuscript review, and final approval. All authors read and approved the final manuscript.

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