International Journal of Clinical Trials
Gupta D et al. Int J Clin Trials. 2026 Nov;13(4):409-417
https://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259
DOI: https://dx.doi.org/10.18203/2349-3259.ijct20262799

Original Research Article

Effect of choline-stabilized orthosilicic acid versus vitamins C and E on peri-implant procollagen type I N-terminal propeptide levels in smokers receiving dental implants: a randomized clinical study

Divya Gupta, Sumit Malhotra*, Aruna Nautiyal, Tanya Attre, Anoushka Pandey, Rahul Chopra

Department of Periodontology and Oral Implantology, ITS Centre for Dental Studies and Research, Muradnagar, Ghaziabad, Uttar Pradesh, India

Received: 05 July 2026
Revised: 03 August 2026
Accepted: 05 August 2026

***Correspondence:**
Dr. Sumit Malhotra,
E-mail: sumitmalhotra@its.edu.in

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Smoking adversely affects peri-implant wound healing, osseointegration, and crestal bone stability through increased oxidative stress and impaired bone metabolism. Nutritional supplementation with bone-forming and antioxidant agents, such as choline-stabilized orthosilicic acid (ch-OSA) and vitamins C and E, may improve implant outcomes in smokers; however, comparative evidence remains limited.
Methods: Twenty-eight smokers undergoing dental implant placement were randomly allocated into two groups. Group A received ch-OSA, while group B received combined vitamin C and vitamin E supplementation for one month postoperatively. Clinical parameters, including plaque index (PI), gingival index (GI), wound healing index (WHI), and implant stability quotient (ISQ), were recorded at baseline and 3 months. Crestal bone levels were assessed using standardized intraoral periapical radiographs at baseline, 1 month, and 3 months. Peri-implant crevicular fluid samples were collected on days 7, 15, and 30 to measure procollagen type I N-terminal propeptide (PINP) levels using ELISA.
Results: Both groups showed significant improvements in clinical parameters and implant stability over time ($p<0.05$), with no significant intergroup differences. Although crestal bone loss occurred in both groups, significantly greater bone loss was observed in the vitamin C and E group at 1 and 3 months ($p<0.05$). PINP levels increased significantly in both groups, with consistently higher values in the ch-OSA group ($p<0.05$).
Conclusions: Ch-OSA supplementation promoted greater bone formation activity and reduced crestal bone loss compared with vit C and E supplementation, suggesting superior support for early peri-implant healing in smokers.

Keywords: Dental implants, Smoking, Choline-stabilized orthosilicic acid, Vitamin C and E, Peri-implant bone loss

INTRODUCTION

Dental implants are a predictable and widely accepted treatment modality for the rehabilitation of partial and complete edentulism, demonstrating high long-term survival rates.[1] However, biological complications such as peri-implant mucositis and peri-implantitis remain prevalent and are significantly influenced by host-related risk factors.[2,3] Among these, cigarette smoking is one of the most consistently identified modifiers of peri-implant tissue healing and marginal bone stability.

Tobacco use continues to be a major global health burden, with more than one billion active smokers worldwide. Smoking has been associated with impaired wound healing, dysregulated immune responses,

increased oxidative stress, and compromised osseointegration.[4] Clinically, smokers demonstrate higher implant failure rates and greater marginal bone loss compared with non-smokers.[5] These adverse outcomes are largely attributed to alterations in bone remodeling, particularly reduced osteoblastic activity.[6] Nicotine has been shown to inhibit osteoblast proliferation, differentiation, and collagen synthesis through nicotinic acetylcholine receptor-mediated pathways.[7] Given the essential role of osteoblasts in type I collagen production and mineralization, smoking may negatively affect early peri-implant bone formation.

Bone turnover markers offer a useful approach for evaluating dynamic changes in bone metabolism.[8] PINP is a sensitive and specific marker of bone formation that reflects osteoblastic activity.[9] In the context of smoking-induced alterations in bone metabolism, assessment of PINP may provide insight into changes in osteoblastic function during peri-implant healing. Peri-implant crevicular fluid (PICF) serves as a non-invasive and site-specific medium for monitoring local biochemical changes associated with peri-implant tissue response.[10]

Although early implant stability is primarily governed by local bone quality and surgical factors, the local biochemical environment may influence subsequent bone remodeling and osseointegration. Smoking-induced oxidative stress further contributes to impaired healing, suggesting a potential role for adjunctive antioxidant therapy.[11] Vitamins C and E are known to support collagen synthesis and mitigate oxidative stress; however, their effects on peri-implant bone metabolism remain inconclusive.[12]

Orthosilicic acid has been implicated in bone metabolism through its role in collagen synthesis and early matrix formation. Choline-stabilized orthosilicic acid (ch-OSA), a bioavailable form, has been shown to enhance type I collagen production and stimulate osteoblastic activity, thereby potentially supporting bone formation and mineralization.[13,14] Given that smoking impairs collagen synthesis and osteoblast function, ch-OSA may offer a targeted approach to modulate these pathways during peri-implant healing. However, clinical evidence evaluating its efficacy in smokers undergoing implant therapy remains limited.

Therefore, the aim of the present randomized clinical study was to compare the effects of ch-OSA and vitamins C and E on peri-implant bone formation in smokers by assessing PINP levels in PICF, along with clinical and radiographic parameters.

METHODS

Study design and ethical approval

This randomized, parallel-arm, clinicoradiographic and biochemical clinical trial was conducted in the Department of Periodontology and Oral Implantology, ITS Centre for Dental Studies and Research, Ghaziabad, India. The study protocol was approved by the institutional ethics committee (Protocol No. ITSCDSR/IIEC/2023-26/PERIO/03) and registered with the Clinical Trials Registry of India. The study was performed in accordance with the declaration of Helsinki (2013 revision). Written informed consent was obtained from all participants prior to enrollment.

Study population

Patients requiring implant placement were screened from the outpatient department. A total of 28 implant sites in light smokers (≤10 cigarettes/day) were included, with a maximum of two sites per patient.

Inclusion criteria

Patients with age 18-60 years, light daily smokers (≤10 cigarettes/day), healed edentulous sites ≥3 months post-extraction, adequate ridge dimensions (≥6 mm width and ≥10 mm height) confirmed by CBCT, absence of active periodontal disease and willingness to comply with study protocol were included in the study.

Exclusion criteria

Patients with uncontrolled systemic diseases (e.g., diabetes mellitus), autoimmune disorders or osteoporosis, history of radiation or chemotherapy within the past 6 months, pregnancy or lactation, acute infection at implant site and use of medications affecting bone metabolism (e.g., bisphosphonates, corticosteroids, anticonvulsants, hormone therapy) were excluded the study.

Sample size calculation

Sample size was calculated using G*Power software (version 3.1.9.7). Based on previous data, a mean difference of 0.9 with a standard deviation of 0.7 was assumed, yielding an effect size of 1.39. With 95% power and a 5% significance level, a minimum of 14 implant sites per group was required (total n=28).

Pre-surgical phase

All participants received phase I periodontal therapy, including oral prophylaxis and oral hygiene instructions. Tobacco cessation counseling was provided. Surgical procedures were performed 2 weeks after initial therapy. Baseline PI and GI scores were recorded on the day of surgery.

Randomization and allocation

Participants were randomly assigned to two groups using a computer-generated randomization sequence. Allocation concealment was maintained using sealed opaque envelopes.

Group A-ch-OSA and group B-vitamin C and E supplementation.

Surgical procedure

All implants were placed under aseptic conditions using a standardized protocol. Patients rinsed with 0.12% chlorhexidine gluconate prior to surgery. Local anesthesia was achieved using 2% lidocaine with 1:100,000 epinephrine.

A mid-crestal incision with sulcular extensions was made, and a full-thickness mucoperiosteal flap was elevated. Osteotomy preparation was performed under copious saline irrigation following the manufacturer's drilling sequence. Implants were inserted to achieve primary stability.

Primary implant stability was measured immediately using resonance frequency analysis (RFA) implant stability quotient (ISQ) (Figure 3). Standardized intraoral periapical radiographs were obtained using the paralleling technique for baseline crestal bone level assessment (Figure 4). Healing abutments were placed, and flaps were sutured using 4-0 silk sutures. Sutures were removed after 7 days (Figure 1 A-E).

Intervention protocol

Group A

Received ch-OSA (BioSil®; 105 mg/day containing 100 mg choline and 5 mg silicon), administered orally in divided doses for 30 days (Figure 2 A).

Group B

Received vitamin C (Limcee®; 500 mg ascorbic acid) and Vitamin E (Evion®; 400 IU tocopherol acetate), administered orally once daily for 30 days (Figure 2 B).

Supplementation commenced on the day of implant placement.

Compliance was reinforced at follow-up visits.

Postoperative care

Standard postoperative instructions were provided. Antibiotics were prescribed for 5 days, and analgesics (paracetamol 500 mg) were given as needed.

Outcome measures and follow-up

Primary outcome

Peri-implant crevicular fluid (PICF) levels of PINP were primary outcomes.

Secondary outcomes

WHI, ISQ, crestal bone level changes and PI and GI secondary outcomes.

PICF collection and biochemical analysis

PICF samples (3 µl) were collected extracrevicularly using calibrated microcapillary pipettes at 7 days, 15 days, and 1 month.

Samples were transferred to Eppendorf tubes containing phosphate-buffered saline and stored at-20°C (-80°C for final analysis) until estimation of PINP levels (Figure 1 F).

Clinical and radiographic assessment

Seven days-WHI and PICF collection. Fifteen days-PICF collection and compliance assessment. One month-WHI, radiographic crestal bone levels, PICF collection. Three months-PI, GI, ISQ measurement, and radiographic bone level assessment.

Crestal bone levels were measured from the implant shoulder to the first bone-to-implant contact using the standardized intra-oral peri-apical radiographs shown in the Figure 4.

Statistical analysis

All data were entered into Microsoft Excel and analyzed using SPSS software (version 21.0; IBM Corp., Armonk, NY, USA).

Data were screened for completeness and accuracy prior to analysis.

Normality of data distribution was assessed using the Shapiro-Wilk test. Based on data distribution, appropriate parametric or non-parametric tests were applied.

For normally distributed data, intergroup comparisons (Group A vs. Group B) of crestal bone loss, ISQ, WHI, and PINP levels at corresponding time points were performed using the independent samples t test.

Intragroup comparisons across time intervals were analyzed using paired t tests for ISQ and WHI, and repeated measures analysis of variance (ANOVA) followed by post hoc least significant difference (LSD) test for crestal bone levels and PINP.

For non-normally distributed data, intragroup comparisons of PI and GI were performed using the Wilcoxon signed-rank test.

All statistical tests were two-tailed, and a $p<0.05$ was considered statistically significant.

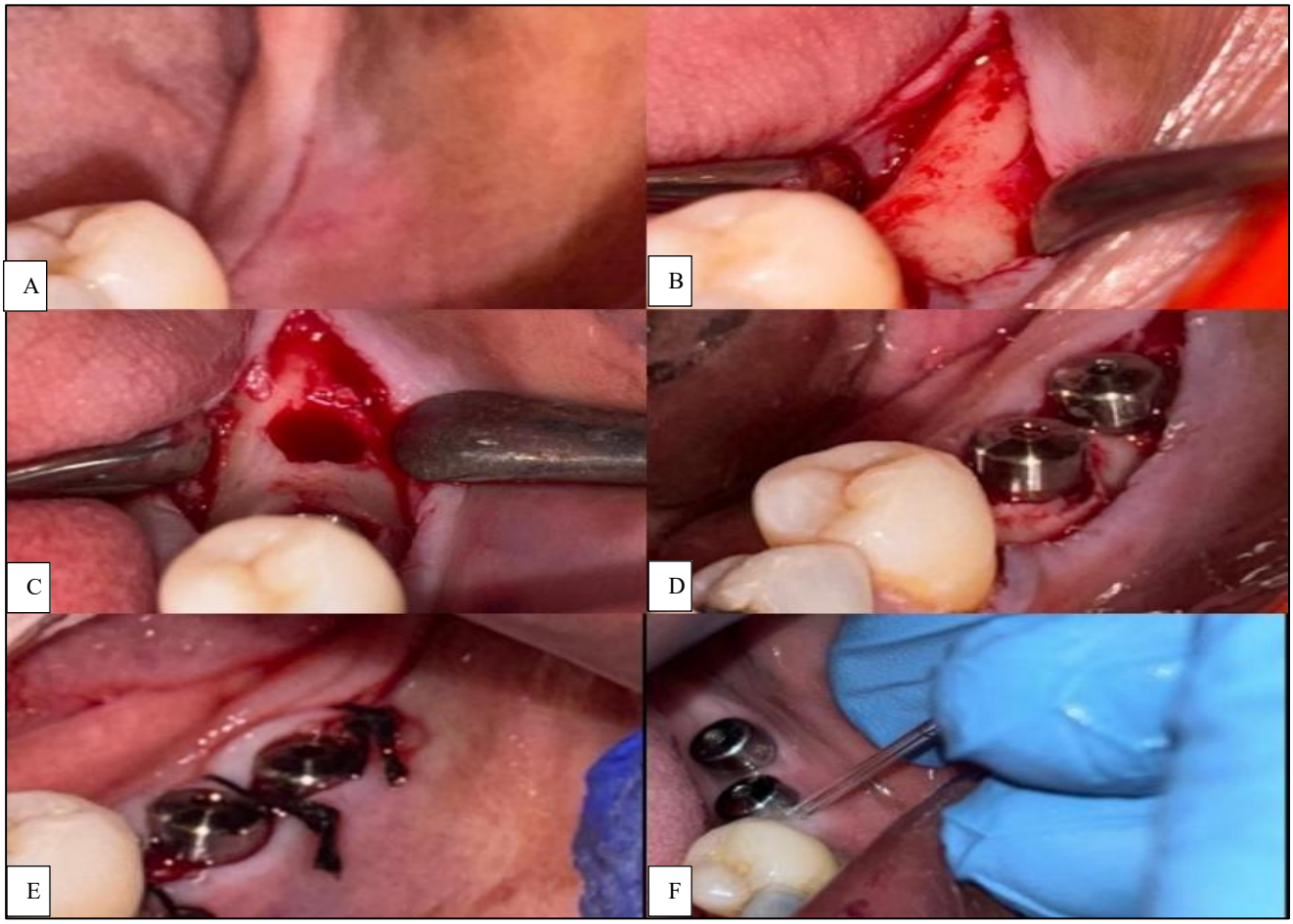


Figure 1 (A-F): Surgical and sampling protocol, (A) Crestal incision line, (B) Full-thickness mucoperiosteal flap reflection, (C) Sequential osteotomy preparation, (D) Placement of healing abutment following implant insertion, (E) Suturing of the surgical site, (F) Collection of peri-implant crevicular fluid at 7 days postoperatively, (Surgical protocol was identical for both groups).



Figure 2 (A and B): **(A) Choline-stabilized orthosilicic acid (BioSil), (B) Vitamin C (Limcee) and vitamin E (Evion) used as antioxidant supplementation in study.**



Figure 3: Implant stability assessment using RFA with a Penguin device to determine ISQ values.

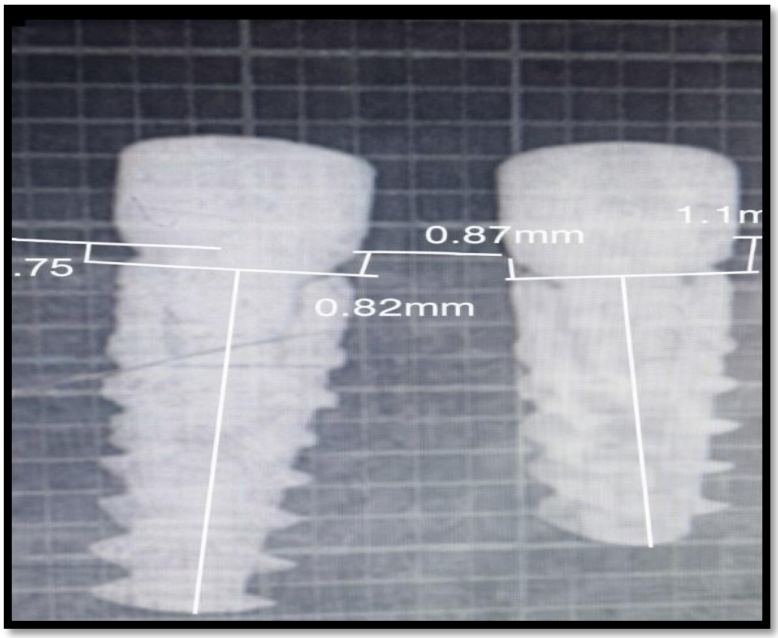


Figure 4: Radiographic assessment of crestal bone level using intraoral periapical radiograph analyzed with ImageJ software.

*Measurements were calibrated using a standardized grid for accurate linear evaluation of peri-implant bone levels.

RESULTS

A total of 28 systemically healthy smokers requiring implant placement were enrolled and randomly allocated into two groups (n=14 each). Group A received choline-stabilized orthosilicic acid along with vitamins C and E, while group B received vitamins C and E alone. No statistically significant differences were observed between the groups at baseline with respect to age or gender distribution (p>0.05) (Table 1).

Plaque and gingival parameters

PI scores showed a significant reduction from baseline to 3 months in both group A (1.68±0.16 to 1.19±0.15) and group B (1.70±0.14 to 1.20±0.13) (p≤0.05), with no significant intergroup differences at any time point (p>0.05) (Table 2).

Similarly, GI scores decreased significantly over time in both group A (1.52±0.17 to 1.04±0.16) and group B (1.50±0.16 to 1.00±0.14) (p≤0.05), without significant intergroup differences at any evaluation point (p>0.05) (Table 2).

Wound healing

WHI scores demonstrated significant improvement from 7 days to 1 month in both group A (2.93±0.47 to 4.71±0.47) and group B (2.79±0.58 to 4.93±0.27) (p≤0.05). However, no statistically significant differences were observed between the groups at either time point (p>0.05) (Table 2).

Implant stability

Implant stability, assessed using ISQ values, increased significantly from baseline to 3 months in both group A (72.14±7.13 to 79.36±7.04) and group B (66.07±9.39 to 71.14±10.74) ($p \leq 0.05$). Intergroup comparisons revealed no statistically significant differences at baseline/at 3 months ($p > 0.05$) (Table 2).

Crestal bone changes

Baseline crestal bone levels comparable between group A (0.45±0.36 mm) and group B (0.47±0.03 mm) ($p > 0.05$). At 1 month, mean bone level changes were-0.06±0.52 mm in group A and -0.56±0.05 mm in B, while at 3 months changes were -0.69±0.33 and -1.14±0.30 mm, respectively. Intergroup analysis demonstrated significantly greater crestal bone loss in group B at both 1 and 3 months ($p < 0.05$). Intragroup analysis revealed a significant progressive increase in bone loss over time in both groups, with a more pronounced effect in group B ($p < 0.05$) (Table 3 and 4).

PINP levels in PICF

PINP levels in peri-implant crevicular fluid increased progressively over time in both groups. In group A, mean values were 2.84±0.12 ng/ml at 7 days, 4.53±0.12 ng/ml at 15 days, and 7.08±0.24 ng/ml at 30 days. In group B, corresponding values were 2.03±0.58 ng/ml, 2.68±1.03 ng/ml, and 3.80±1.35 ng/ml, respectively.

Group A demonstrated significantly higher PINP levels at all time points compared to group B ($p \leq 0.05$), with statistically significant increases observed within both groups over time ($p < 0.05$) (Table 5 and 6).

Table 1: Demographic details.

Variables		Group A	Group B
Age (in years)	-	42.13±7.99	39.88±13.69
Gender	Male	12 (85.7%)	11 (78.5%)
	Female	2 (14.2%)	3 (21.4%)

Table 2: Intragroup and intergroup comparison of PI, GI, WHI, ISQ.

Clinical parameters	Time point	Group A, (Mean±SD)	Group B, (Mean±SD)	Intragroup, p value	Intergroup, p value
PI	Baseline	1.68±0.16	1.70±0.14	<0.05**	>0.05
	3 months	1.19±0.15	1.20±0.13		>0.05
	Difference	0.49±0.03	0.50±0.00		
GI	Baseline	1.52±0.17	1.50±0.16	<0.05**	>0.05
	3 months	1.04±0.16	1.00±0.14		>0.05
	Difference	0.48±0.04	0.50±0.00		
WHI	7 days	2.93±0.47	2.79±0.58	<0.05**	>0.05
	1 month	4.71±0.47	4.93±0.27		>0.05
	Difference	1.79±0.58	2.14±0.53		
ISQ	Baseline	72.14±7.13	66.07±9.39	<0.05**	>0.05
	3 months	79.36±7.04	71.14±10.74		>0.05
	Difference	7.21±5.78	5.07±4.83		

*Independent samples t-test; **indicates $p < 0.05$.

Table 3: Intergroup comparison of radiographic bone height (in mm) at baseline, 1 month and 3 months.

Time points	Group A		Group B		Difference	P value
	Mean	SD	Mean	SD		
Baseline	0.45	0.36	0.47	0.03	-0.02	>0.05
1 month	-0.06	0.52	-0.56	0.05	0.48	<0.05 **
3 months	-0.69	0.33	-1.14	0.30	0.47	<0.05**

*Independent samples t-test; **indicates $p < 0.05$.

Table 4: Intragroup comparison of radiographic bone height (in mm) at baseline, 1 month and 3 months.

Groups	Intervals	Mean	SD	P value	Pairwise comparison
Group A	**Baseline**	0.45	0.36	<0.05*	Baseline v/s 1 month: p>0.05 Baseline v/s 3 months: p≤0.05** 1 month v/s 3 months: p≤0.05**
	1 month	-0.06	0.52		
	3 months	-0.69	0.33		

Continued.

Groups	Intervals	Mean	SD	P value	Pairwise comparison
Group B	Baseline	0.47	0.03	<0.05*	Baseline v/s 1 month: p≤0.05**
	1 month	-0.56	0.05		baseline v/s 3 months: p≤0.05**
	3 months	-1.14	0.30		1 month v/s 3 months: p≤0.05**

*Repeated measures ANOVA test; Least Significant Difference; **indicates a significant difference at p≤0.05

Table 5: Intergroup comparison of PINP levels (in ng/ml) at 7 days, 15 days and 30 days.

Time points	Groups	N	Mean±SD	T value	P value
7 days (PINP7)	Group A	14	2.84±0.12	5.092	<0.05**
	Group B	14	2.03±0.58		
15 days (PINP15)	Group A	14	4.53±0.12	6.689	<0.05**
	Group B	14	2.68±1.03		
30 days (PINP30)	Group A	14	7.08±0.24	8.975	<0.05**
	Group B	14	3.80±1.35		

*Independent t test; **indicates a significant difference at p≤0.05

Table 6: Intragroup comparison of PINP levels (in ng/ml) at 7 days, 15 days and 30 days.

Groups	Intervals (days)	Mean	SD	P value	Pairwise comparison
Group A	7	2.84	0.12	<0.05**	7 days v/s 15 days: p≤0.05**
	15	4.53	0.12		15 days v/s 30 days: p≤0.05**
	30	7.08	0.24		7 days v/s 30 days: p≤0.05**
Group B	7	2.03	0.58	<0.05**	7 days v/s 15 days: p≤0.05**
	15	2.68	1.03		15 days v/s 30 days: p≤0.05**
	30	3.80	1.35		7 days v/s 30 days: p≤0.05**

*Repeated measures ANOVA test; least significant difference; ** indicates a significant difference at p≤0.05

DISCUSSION

The present randomized clinical trial evaluated the effect of ch-OSA compared with vitamin C and vitamin E supplementation on peri-implant bone metabolism in light smokers, using peri-implant crevicular fluid (PICF) levels of PINP as a marker of early bone formation.

PI and GI scores showed significant improvement over time in both groups, with no intergroup differences. These findings are consistent with the observations of Silness and Löe, who reported that plaque-related parameters primarily reflect oral hygiene status rather than systemic modulation. The absence of intergroup differences suggests that both groups benefited equally from standardized maintenance protocols, indicating minimal influence of supplementation on peri-implant soft tissue plaque control.[16]

WHI scores improved significantly from 7 days to 1 month in both groups without significant intergroup differences. Vitamin C is known to support collagen hydroxylation and angiogenesis during early wound repair, as previously reported by Vandana et al and Li et al.[17,18] However, similar healing outcomes in both groups suggest that surgical protocol and local tissue factors play a more dominant role in early peri-implant soft tissue healing than systemic supplementation. Thus, the adjunctive effect of vitamins on early healing in the present study appears limited.

ISQ increased significantly over time in both groups, reflecting the expected transition from primary to secondary stability during osseointegration. Similar ISQ progression in smokers without supplementation has been reported previously, indicating that early implant stability is largely governed by local bone quality and surgical factors.[19] Although silicon has been shown to enhance osteoblastic differentiation and collagen synthesis experimentally, these effects may not translate into measurable differences in short-term clinical implant stability.[20] The lack of intergroup differences is therefore consistent with the understanding that systemic micronutrient modulation has limited influence on early mechanical stability.[21]

Baseline radiographic bone levels were comparable between groups, confirming uniform initial conditions. At 1 and 3 months, however, significantly greater crestal bone loss was observed in the vitamin C and E group compared with the ch-OSA group. Although early marginal bone remodeling is a physiological process, smoking is known to exacerbate osteoclastic activity and impair osteoblastic function, leading to increased bone resorption.[22]

Experimental evidence by Reffitt et al demonstrated that orthosilicic acid enhances type I collagen synthesis and osteoblast differentiation, providing a biological basis for the reduced crestal bone loss observed in the ch-OSA group.[23] Clinical studies by Singh et al and Nazeer et al

have reported higher early marginal bone loss in smokers without adjunctive metabolic support, further supporting the findings of the present study.[24,25] Additionally, Teughels et al observed improved peri-implant bone preservation with ch-OSA supplementation over short-term follow-up, supporting its potential role in early bone remodeling modulation.[26]

In contrast, the vitamin C and E group demonstrated greater crestal bone loss. While antioxidants may reduce oxidative stress-mediated bone resorption, their primary effect is anti-resorptive rather than osteoinductive. Vallibhakara et al reported that vitamin E supplementation reduces bone resorption markers without significantly increasing bone formation markers such as PINP, which may explain the limited effect on marginal bone preservation observed in the present study.[27]

The primary outcome, PINP levels in PICF, demonstrated a progressive increase over time in both groups, reflecting active collagen synthesis during early osseointegration.[28] However, PINP levels were significantly higher in the ch-OSA group at all time points. These findings are consistent with systemic observations by Spector, who reported increased PINP levels following silicon supplementation, suggesting stimulation of collagen turnover and bone formation.[15]

Conversely, longer-term studies have reported attenuation of this effect over extended follow-up periods, indicating that the influence of silicon-based supplementation may be most pronounced during early remodeling phases.[26] The early sampling intervals in the present study (7, 15, and 30 days) likely captured this initial biological response at the peri-implant interface.

Within the limitations of the relatively small sample size, short follow-up period, and absence of a non-supplemented control group, the present findings suggest that ch-OSA may exert a more favorable influence on early peri-implant bone formation compared with antioxidant supplementation alone in smokers. The higher PINP levels and reduced early crestal bone loss in the ch-OSA group indicate enhanced early bone matrix formation during the critical phase of osseointegration.

CONCLUSION

Within the limitations of the present study, both ch-OSA and vitamin C and E supplementation demonstrated favorable effects on peri-implant soft tissue healing, implant stability, and biochemical markers of bone formation in smokers. However, ch-OSA supplementation was associated with significantly higher PINP levels and reduced early crestal bone loss compared with antioxidant supplementation alone.

These findings suggest a potential adjunctive role of ch-OSA in enhancing early peri-implant bone formation in smokers. Nevertheless, further long-term randomized clinical trials with larger sample sizes are required to validate these findings and establish their clinical relevance.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee Institutional independent ethics committee (IIEC), I.T.S. Centre for Dental Studies and Research, Muradnagar, Ghaziabad, Uttar Pradesh, India (Approval No. ITSCDSR/IIEC/2023-26/PERIO/03).

REFERENCES

1. Brånemark PI, Hansson BO, Adell R, Breine U, Lindström J, Hallén O, et al. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. Scand J Plast Reconstr Surg. 1977;16:1-132.
2. Heitz-Mayfield LJA, Salvi GE. Peri-implant mucositis and peri-implantitis. J Clin Periodontol. 2018;45(20):S246-63.
3. Berglundh T, Armitage G, Araujo MG, Avila-Ortiz G, De Bruyn H, Figuero E, et al. Peri-implant diseases and conditions: Consensus report of workgroup 4 of the 2017 World Workshop. J Clin Periodontol. 2018;45(20):S286-91.
4. Strietzel FP, Reichart PA, Kale A, Kulkarni M, Wegner B, Küchler I. Smoking interferes with the prognosis of dental implant treatment: a systematic review and meta-analysis. J Clin Periodontol. 2007;34(6):523-44.
5. Baig MR, Rajan M. Effects of smoking on the outcome of implant treatment: a literature review. Indian J Dent Res. 2007;18(4):190-5.
6. Bain CA, Moy PK. The association between failure of dental implants and cigarette smoking. Int J Oral Maxillofac Implants. 1993;8:609-15.
7. Ward KD, Klesges RC. A meta-analysis of the effects of cigarette smoking on bone mineral density. Osteoporos Int. 2001;12(12):1050-7.
8. Liang D, Wang KJ, Tang ZQ, Liu RH, Zeng F, Cheng MY, et al. Effects of nicotine on metabolism and gene expression of rat osteoblasts. Mol Med Rep. 2018;17(6):8269-81.
9. Ram VS, Parthiban S, Sudhakar U, Mithradas N, Prabhakar R. Bone biomarkers in periodontal disease: a review. J Clin Diagn Res. 2015;9(1):ZE07-10.
10. Hale LV, Sells Galvin RJ, Risteli J, et al. PINP: a serum biomarker of bone formation in the rat. Bone. 2007;40(4):1103-9.
11. Schwarz F, Derks J, Monje A, Wang HL. Biomarkers from peri-implant crevicular fluid as predictors of peri-implant bone loss: a systematic review. Int J Mol Sci. 2023;24(4):3202.
12. Qi F, Huang H, Wang M, Rong W, Wang J. Applications of antioxidants in dental procedures. Antioxidants. 2022;11(12):2492.

13. Traber MG, Stevens JF. Vitamins C and E: beneficial effects from a mechanistic perspective. Free Radic Biol Med. 2011;51(5):1000-13.
14. Prabhoo R. Choline-stabilized orthosilicic acid and bone health. Curr Med Issues. 2020;18(4):312-6.
15. Spector TD, Calomme MR, Anderson SHC, Clement G, Bevan L, Demeester N, et al. Choline-stabilized orthosilicic acid supplementation stimulates markers of bone formation in osteopenic females. BMC Musculoskelet Disord. 2008;9:85.
16. Löe H, Silness J. Periodontal disease in pregnancy I. Prevalence and severity. Acta Odontol Scand. 1963;21:533-51.
17. Vandana S, Goyal P, Singh ST, Kaur S, Suchdev V. Vitamin C supplementation in wound healing post dental implant surgery. J Pharm Res Int. 2023;35(33):1-7.
18. Li X, Tang L, Lin YF, Xie GF. Role of vitamin C in wound healing after implant surgery. Clin Implant Dent Relat Res. 2018;20(5):793-8.
19. Tüter G, Yildirim AZ, Duman AN, Behruz A, Atak-Yucel A, Oruklu N, et al. Smoking effect on bone ALP and implant stability. Odontology. 2022;110(3):596-604.
20. Jugdaohsingh R, Reffitt DM, Oldham C, Cheung HFJ, Evans BAJ, Thompson RPH, et al. Orthosilicic acid stimulates collagen type I synthesis. Bone. 2003;32(2):127-35.
21. Javed F, Romanos GE. Role of primary stability for implant success. J Dent. 2010;38(8):612-20.
22. Mumcu E, Beklen A. Smoking and marginal bone loss around implants. Tob Induc Dis. 2019;17:43.
23. Reffitt DM, Ogston N, Jugdaohsingh R, Cheung HFJ, Evans BAJ, Thompson RPH, et al. Orthosilicic acid and osteoblast differentiation. Bone. 2003;32(2):127-35.
24. Singh S, Bhoi S, Parmar H. Marginal bone loss in smokers vs non-smokers. J Oral Biol Craniofac Res. 2023;13(2):145-50.
25. Nazeer J, Singh R, Suri P, Mouneshkumar CD, Bhardwaj S, Iqubal MA, et al. Evaluation of marginal bone loss around dental implants in cigarette smokers and nonsmokers. A comparative study. J Family Med Prim Care. 2020;9(2):729-34.
26. Teughels W, Celik E, Tarce M, Cock ID, Persyn SM, Haytac MC. The effect of choline-stabilized orthosilicic acid in patients with peri-implantitis: an exploratory randomized, double-blind, placebo controlled study. Clin Oral Investig. 2021;25(2):673-83.
27. Vallibhakara O, Nakpalat K, Sophonsritsuk A. Tocopherols and bone turnover markers. J Obstet Gynaecol Res. 2021;47(7):2343-50.
28. Gillett MJ, Vasikaran SD, Inderjeeth CA. PINP in metabolic bone disease. Clin Biochem Rev. 2021;42(1):3-10.

Cite this article as: Gupta D, Malhotra S, Nautiyal A, Attre T, Pandey A, Chopra R. Effect of choline-stabilized orthosilicic acid versus vitamins C and E on peri-implant procollagen type I N-terminal propeptide levels in smokers receiving dental implants: a randomized clinical study. Int J Clin Trials 2026;13(4):409-17.