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Locally Delivery of Minocycline Immediately After Implant Surgery: A 12-Week Randomized Controlled Clinical Trial

Yanjun Zhang, Xingmei Yang, Quan Yuan*. State Key Laboratory of Oral Diseases & National Clinical Research Center for Oral Diseases & Department of Implant，West China Hospital of Stomatology，Sichuan University，Chengdu，China.

Abstract

Background: The aim of this randomized controlled clinical trial is to determine the clinical and microbial effects of local delivered minocycline hydrochloride ointment immediately after implant surgery.

Materials and Methods: Forty partially edentulous patients were recruited and randomly assigned to two groups: test group (minocycline hydrochloride treatment group); control group(blank control). Pain index was measured at 3 days after surgery. Gingival index (GI), modified Sulcus Bleeding Index (mSBL) and peri-implant crevicular fluid samples were measured and collected at 3 and 7 days after surgery. IL-1β, IL-10 and TNF-α concentrations were measured by enzyme linked immunosorbent assay (ELISA). Microbial analysis was performed with real-time polymerase chain reaction. The change of marginal bone level (MBL) measured with panoramic radiograph was analyzed between immediately and 12 weeks after surgery.

Results: The results of pain index, GI and mSBL in the test group were significantly lower than in the control group (P=0.03, 0.005 and 0.015, respectively) at 3 days, and (P＜0.001) at 7 days. The concentration of IL-1β, IL-10 and TNF-α were significantly lower in the test group (P=0.016, 0.034 and 0.045, respectively) at 3 days. The relative abundance of streptococcus and gram-negative anaerobic bacteria was significantly lower in the test group (P=0.011 and ＜0.001, respectively) at 3 days, and (P=0.017 and ＜0.001, respectively) at 7 days after surgery. There was no significantly difference of MBL between the test and control group.

Conclusion: These findings indicated that the local delivery of minocycline provides significant benefits in terms of reducing postoperative pain, promoting wound healing and decreasing gram-negative anaerobic bacteria early colonization.

Figures

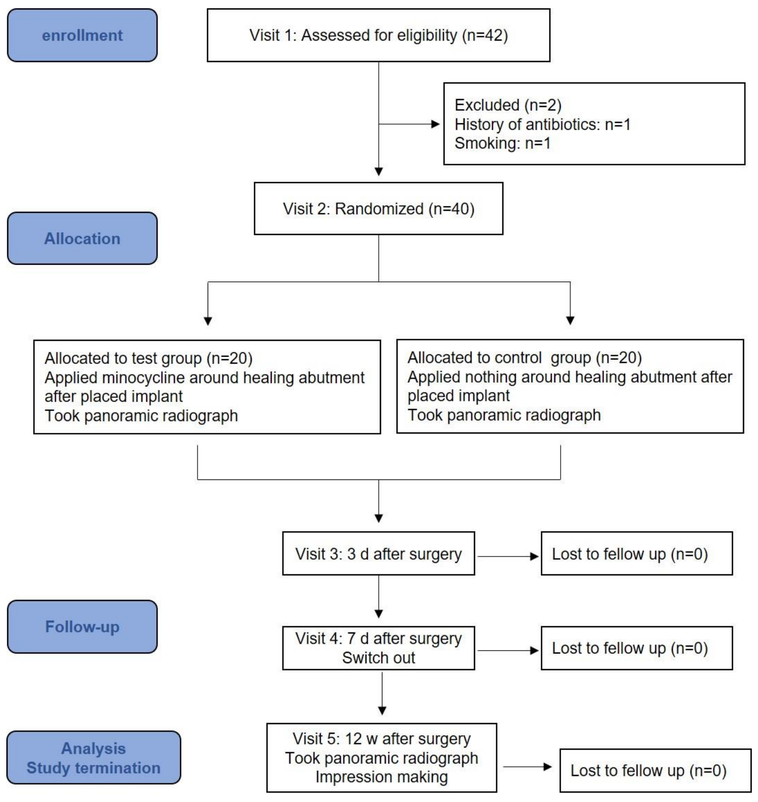

Figure 1 CONSORT flowchart of the study

Table 1 Demographic characteristics on patients

	All groups	Control	Test
Patients	40	20	20
Mean age, y, (range)	38.3 (20 to 62)	41.1 (20 to 62)	35.2 (20 to 59)
Gender			
Male	15 (37.5)	7 (35)	8 (40)
Female	25 (62.5)	13 (65)	12 (60)
Jaw			
Maxilla	15	8 (40)	9 (45)
Mandibula	25	12 (60)	11(55)

Values are presented as *n* (%) unless noted otherwise. *P* > 0.05 for all intergroup comparisons.

Figure 2 Clinical photographs. (A) Minocycline application immediately after surgery. (B)Revisit at 3 d after surgery. (C)Revisit at 7 d after surgery.

Table 2 Results of clinical parameters at 3 days after implant surgery

	control	test	P value
Pain index	2.21±2.10	0.94±0.93	0.03*
Gingival index	1.79±0.63	1.1±0.79	0.005*
modified Sulcus Bleeding Index	1.05±0.85	0.45±0.61	0.015*

Values are presented as mean ± SD.
*Significant difference between the test and control groups (*P* < 0.05).

Table 3 Results of clinical parameters at 7 days after implant surgery

	control	test	P value
Gingival index	1.75±0.85	0.45±0.69	< 0.001*
modified Sulcus Bleeding Index	1.1±0.72	0.1±0.31	< 0.001*

Values are presented as mean ± SD.
*Significant difference between the test and control groups (*P* < 0.05).

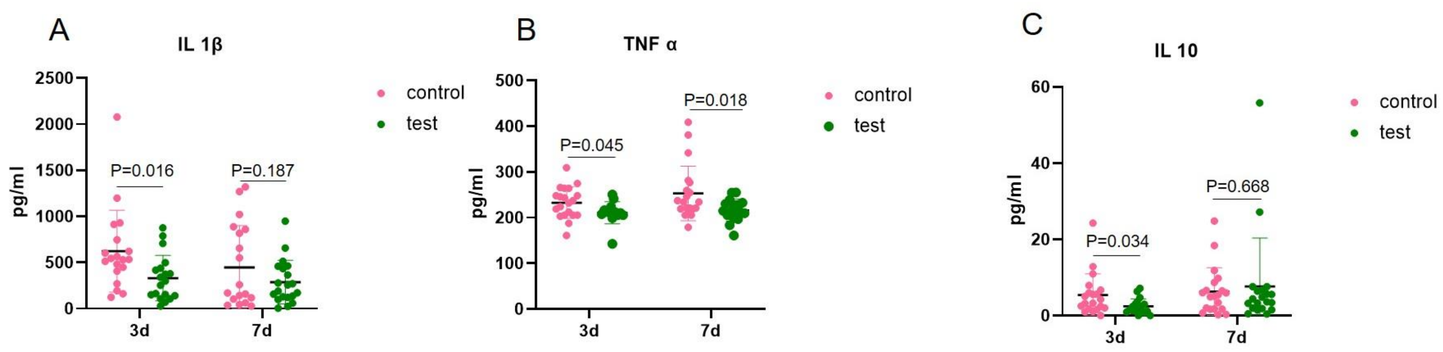

Figure 3 minocycline decreased IL-1β, IL-10, TNF-α concentrations in peri-implant crevicular at 3 and 7 days after surgery. (A) IL-1β concentration in PICF at 3 and 7 d after surgery (P=0.016 and 0.187, respectively). (B) TNF-α concentration in PICF at 3 and 7 d after surgery (P=0.045 and 0.018, respectively). (C) IL-10 concentration in PICF at 3 and 7 d after surgery (P=0.034 and 0.668, respectively).

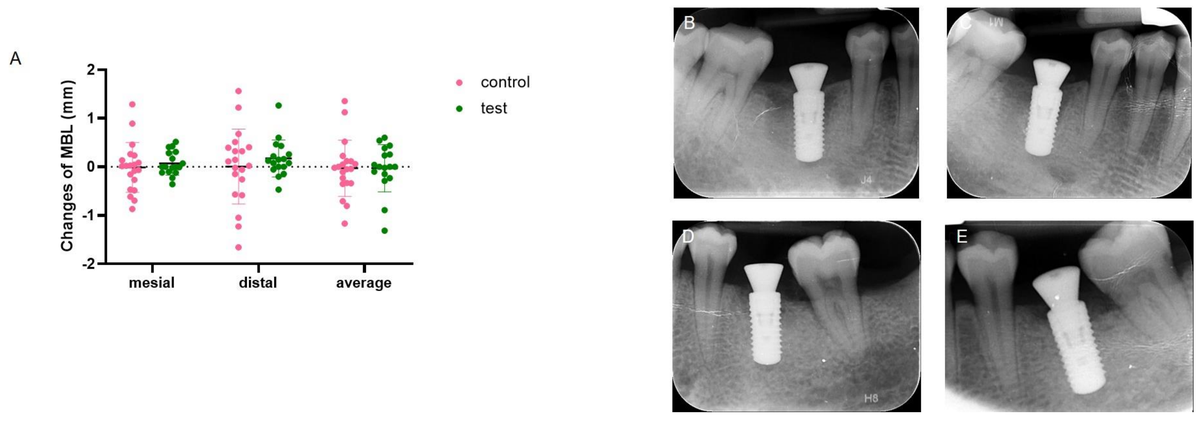

Figure 4 Effect of minocycline on marginal bine level. (A)Changes of MBL at 12 weeks after implant surgery (B) Radiographs of control group immediately after surgery. (C)Radiographs of control group12 weeks after surgery. (D) Radiographs of test group immediately after surgery. (E) Radiographs of test group12 weeks after surgery

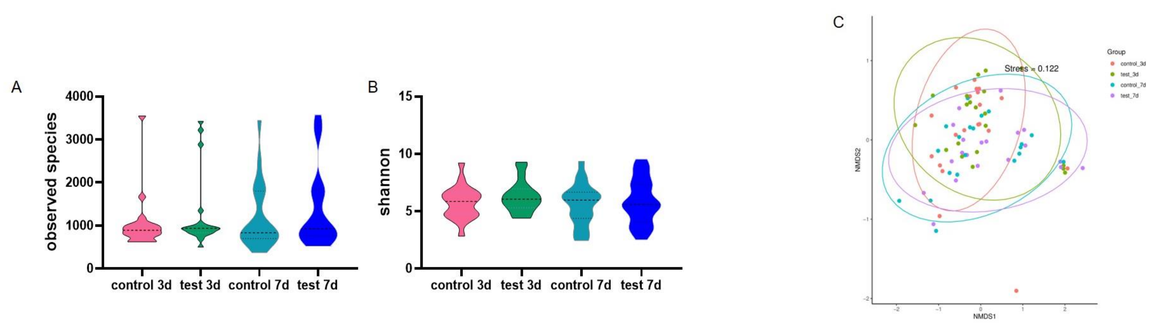

Figure 5 Alpha and beta diversity of peri-implant microbes. (A) Observed species comparing the control to test group for combined 3 d and 7 d. (B) Shannon diversity index comparing the control to test group for combined 3 d and 7 d. (C) NMDS comparing the control to test group for combined 3 d and 7 d.

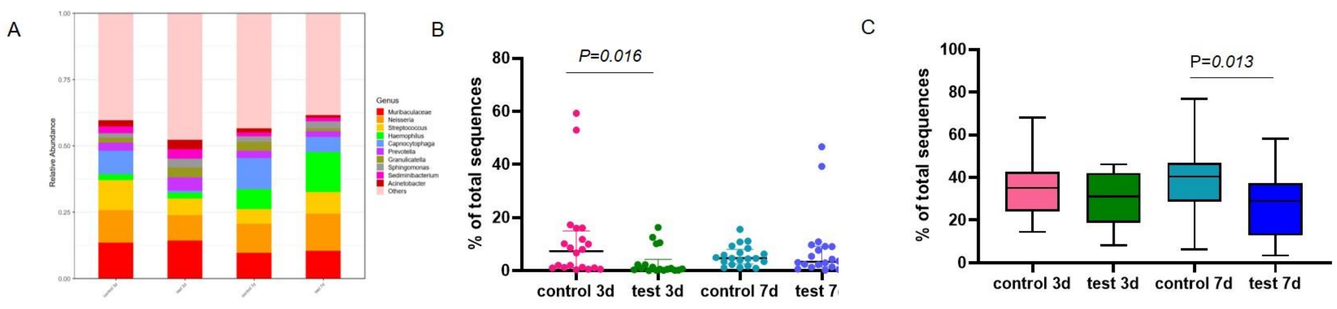

Figure 6 Relative abundance of peri-implant microbes. (A) Relative abundance of top ten genera. (B) Relative abundance of Streptococcus genus at 3 and 7 d after surgery. (C) Relative abundance of gram-negative anaerobic bacteria at 3 and 7 d after surgery.