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Do postoperative antibiotics influence one-year peri-implant crestal bone remodelling and morbidity? A double-blinded randomized clinical trial

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Abstract

Objectives: The primary objective of this study was to assess whether giving postoperative antibiotics to healthy patients after straightforward platform-switched implant placement would influence peri-implant crestal bone levels and postoperative morbidity after 1 year.

Methods: Thirty-eight healthy individuals were recruited in this pilot, randomized, double-blinded, placebo-controlled clinical trial. The intervention group ($n = 18$) received two grams of amoxicillin one hour before implant placement followed by a 7 days postoperative regimen (500 mg tid). The control group ($n = 20$) took the same preoperative dose of amoxicillin and an identical placebo postoperatively. Mesial and distal peri-implant crestal bone levels were measured at baseline, four months and one year later with standardized periapical radiographs. Postoperative pain severity was assessed through self-administered questionnaires for 7 days. Surgery-associated morbidities were evaluated after one, three, 16 weeks and 1 year. Descriptive and bivariate analyses were used.

Results: Thirty-seven participants completed the trial. At the one-year follow-up, the mean combined peri-implant crestal bone changes for the intervention ($n = 18$) and control ($n = 19$) groups were - 0.44 ± 0.41 mm and - 0.27 ± 0.56 mm, respectively. The difference between the groups (intervention–control) for mean combined crestal bone level changes was not statistically significant. There were no significant differences in surgery-associated morbidities between the intervention and control groups. The one-year implant survival rate was 100% in both groups.

Conclusions: Study results suggest that a routine postoperative antibiotic regimen for healthy patients undergoing straightforward platform-switched implant placement might not be necessary to prevent postoperative peri-implant bone loss and complications.

KEYWORDS
clinical research, clinical trials, drug delivery, patient-centred outcomes, pharmacology, wound healing

1 | INTRODUCTION

Antibiotics are widely used in dentistry to treat numerous infections. However, the overuse or misuse of antibiotics may cause increased bacterial resistance as seen in countries where they can be purchased over the counter (van Winkelhoff et al., 2000). Dental implants are becoming increasingly popular to rehabilitate missing dentition due to their numerous advantages. To increase implant success rate and reduce the risk of postoperative complications, it was initially proposed to use a two grams preoperative dose of amoxicillin before implant placement (Adell and Branemark, 1985). Several antibiotic regimens have been proposed thereafter. A clear lack of standardization among perioperative antibiotic regimens in oral implantology used by dental professionals was observed in five countries (Rodriguez Sanchez et al., 2020). Therefore, there is clearly a need to determine a valid perioperative antibiotic regimen in implantology.

Clinical studies have shown conflicting results regarding the effects of peri-operative use of antibiotics on implant survival rate. A complex systematic review reported that peri-operative antibiotics in conjunction with implant placement reduced the risk for implant loss by 2% and has suggested that there is no benefit to prescribe antibiotics in uncomplicated implant surgery in healthy patients (Lund et al., 2015) while the latest Cochrane review concluded that preoperative antibiotics given one hour before implant placement surgery significantly reduced implant failure rates in general (Esposito et al., 2013). However, the authors were unable to determine whether it was beneficial to prescribe postoperative antibiotics in addition to a prophylactic regimen due to a lack of published data. Perioperative antibiotic use has been shown to decrease implant failure rate in a recent systematic review and network meta-analysis (Romandini et al., 2019). The authors concluded that there was insufficient evidence to recommend a specific dosage and the use of postoperative antibiotics did not provide any benefit in terms of implant loss but was associated with increased adverse events. However, the studies included presented a high risk of bias and very few used placebo controls, subject-based outcomes and follow-ups longer than four months.

Asides from dental implant failure, a way to determine whether perioperative antibiotics have a positive effect on the patient's oral health is to evaluate crestal bone loss around the implant. It has been shown that patients who were taking antibiotics postoperatively had less peri-implant crestal bone loss after six months of implant placement compared with those who did not receive any postoperative antibiotics (Manz, 2000). However, there are very little data available on the influence of antibiotics on crestal bone-level change. In addition, very few controlled clinical trials have examined the effects of different antibiotic regimens on patient-based outcomes such as pain and morbidity. Hence, the aim of this two-arm double-masked randomized clinical trial was to evaluate the influence of postoperative antibiotics on peri-implant crestal bone remodelling after one year, postoperative pain and morbidity and one-year implant survival rate in healthy patients undergoing straightforward platform-switched implant placement.

2 | MATERIALS AND METHODS

2.1 | Participants, eligibility criteria and ethical issues

The study used a double-masked two-arm randomized controlled clinical trial (ClinicalTrials.gov Identifier: NCT01851681). Fifty patients from the implantology clinic at the Université de Montréal were invited to participate in the study by a research assistant. The eligibility criteria are presented in Table 1. Eligible participants were randomized in two groups using block randomization. It was done in blocks of six subjects by a computer-generated sequence (PROC PLAN in SAS version 9.4 [SAS Institute Inc.]). The subject allocation was determined before the study enrolment by a research assistant who was not involved in the data collection and analysis, and it remained sealed in consecutively numbered opaque envelopes kept in a locked cabin. The surgeons, participants and examiners were all unaware of subject allocation throughout the study. All study procedures were performed in accordance with the Helsinki Declaration and its later amendments, and all participants signed an informed consent prior to their participation (Université de Montréal Ethics Committee Certificate #13-094-CERES-D). The article preparation follows CONSORT guidelines/checklist as per EQUATOR reporting guidelines for randomized trials.

2.2 | Surgical procedure, prescriptions and postoperative care

All participants were given 600 mg of ibuprofen and two grams of amoxicillin and were instructed to rinse with 0.12% chlorhexidine gluconate for one minute, one hour prior surgery. Standard measures of asepsis included the use of sterile drapes around the patient's head and over the supine body of the patient as well as sterile scrubs and gloves for the surgeon. Screw-type, two-piece dental implants with a moderately rough surface (OsseoSpeed TX™ or Astra EV™, Dentsply Sirona Inc.) were placed in a one-stage procedure without simultaneous bone grafting by two board-certified specialists who had a minimum of 10 years of experience in surgical implantology and according to the manufacturer's recommendations. The healing

TABLE 1 Inclusion and exclusion criteria

Inclusion criteria:
Periodontally healthy remaining dentition or presenting with gingivitis with adequate oral hygiene.
Presence of a partially edentulous alveolar ridge that will be restored with no more than two adjacent implants.
Individuals requiring one or two implant placements
Absence of any active infection.
Presence of enough bone and soft tissue for the implant to be placed without any bone grafting procedure in a one-stage approach (with the placement of a healing abutment).
Implants 8 mm long or longer using the Dentsply AstraTech Implant System™ (OsseoSpeed TX or EV™).
Individuals able and willing to provide written informed consent and comply with study procedures.
Exclusion criteria
Individuals taking regular analgesics or antidepressants.
Allergies to amoxicillin, cephalosporins and non-steroidal anti-inflammatory analgesics.
Smoking ten cigarettes/cigars or more per day.
Drug abuse.
Completely edentulous individuals.
Pregnant and nursing women.
Individuals who have an active peptic ulcer or are susceptible to peptic ulcers.
Any systemic or local immunodeficiency.
Individuals with any blood coagulation impairment or taking anticoagulants (ex.: Coumadin).
Presence of untreated periodontitis or poor oral hygiene.
Presence of any acute oral infection.
Presence of uncontrolled diabetes or other systemic diseases.
Individuals who have received previous radiation therapy in the head and neck area.
Individuals who receive intravenous bisphosphonates.
Individuals who have been taking oral bisphosphonates for more than 3 years.
Individuals with long-term intake of corticosteroids.
Individuals who need routine prophylactic antibiotics prior to dental surgery.
Individuals who have taken antibiotics three months prior to surgery.

abutment was inserted at the time of implant placement, and the soft tissues were adapted and sutured with interrupted sutures (4–0 silk, Perma Sharp™, Hu-Friedy Mfg Co.). All participants were prescribed 600 mg of ibuprofen to be taken every four hours for the first 48 h with a maximum of four tablets per day. They were also prescribed a supplemental dose of analgesic (500 mg acetaminophen) to be taken only if needed. A 0.12% chlorhexidine gluconate rinse was prescribed and was to be used twice daily until the sutures were removed at the one week postoperative appointment. Individuals in the intervention group received 500 mg of amoxicillin three times a day for 7 days after the surgery while the control group received an identical placebo capsule to be taken at the same frequency. The placebo was identical in appearance, dimension, colour, taste and texture and was obtained from a local pharmacy. Daily diaries were given to participants to evaluate their pain and morbidity for the first postoperative week. They were asked to bring back the drugs and diaries at the 1-week follow-up. All implants were restored with fixed prosthesis after the four-month follow-up visit.

2.3 | Radiographic, self-reported and clinical evaluation

Peri-implant crestal bone levels were measured using standardized periapical radiographs at baseline, four-month and 1-year follow-ups. The X-ray cone was positioned perpendicular to the long axis of the implant using a bite registration material (Blu-Mousse, Parkell Inc.) adapted to a paralleling device (RINN XCP® film holding system, Dentsply Sirona Inc.). The same radiographic equipment was used at the same settings for all radiographs. At the 1-year follow-up, since crowns were present on the implants, only the opposing part of the bite registration material was kept to take the radiographs. The radiographic images were sent to the Medical Research Center of the Université de Montréal (CR-CHUM) in order to be repositioned, so the baseline image could be superimposed to the four-month and 1-year images. They were digitally manipulated in a MATLAB environment (MathWorks®) by an expert. The pixel values were compared by using an image similarity measure based on image statistics.

Once the images were processed, an examiner evaluated the crestal bone level by using a standardized method. Using Adobe Photoshop CC 2018 (Adobe Systems Inc.), the examiner drew vertical line using medial points as reference to assure precise alignment with the long axis of the implant. That line was then replicated and rotated at 90 degrees in order to get a precise horizontal axis to measure the peri-implant crestal bone level mesially and distally. Once these lines were drawn, the images were superimposed and the distances between the baseline, the four month and one year postoperative images were measured at high magnification (Figure 1). The mean between mesial and distal crestal bone changes was computed for each implant, and a mean of both implants was calculated per patient.

Self-reported daily postoperative pain severity and surgery-associated morbidities including interference with routine activities were assessed in a daily diary with a 10 cm VAS questionnaire (0–10) to be filled during the first postoperative week. The one-week follow-up included an evaluation of postoperative swelling using a form graded as follows: 0: no swelling, 1: mild swelling, 2: moderate swelling and 3: severe swelling. Postoperative bruising, suppuration and wound dehiscence were evaluated dichotomously. Participants were asked to report any adverse events at the follow-up appointment to the examiner. The three-week follow-up visit included an assessment of the modified plaque index (mPI) (Mombelli et al., 1987), postoperative swelling, bruising, suppuration and wound dehiscence. The four-month and one-year examinations included mPI evaluation as well as implant evaluation using the Albrektsson implant success criteria (Albrektsson et al., 1986). The standardized periapical radiographs were evaluated to confirm the absence of radiolucent lesions. Implant mobility

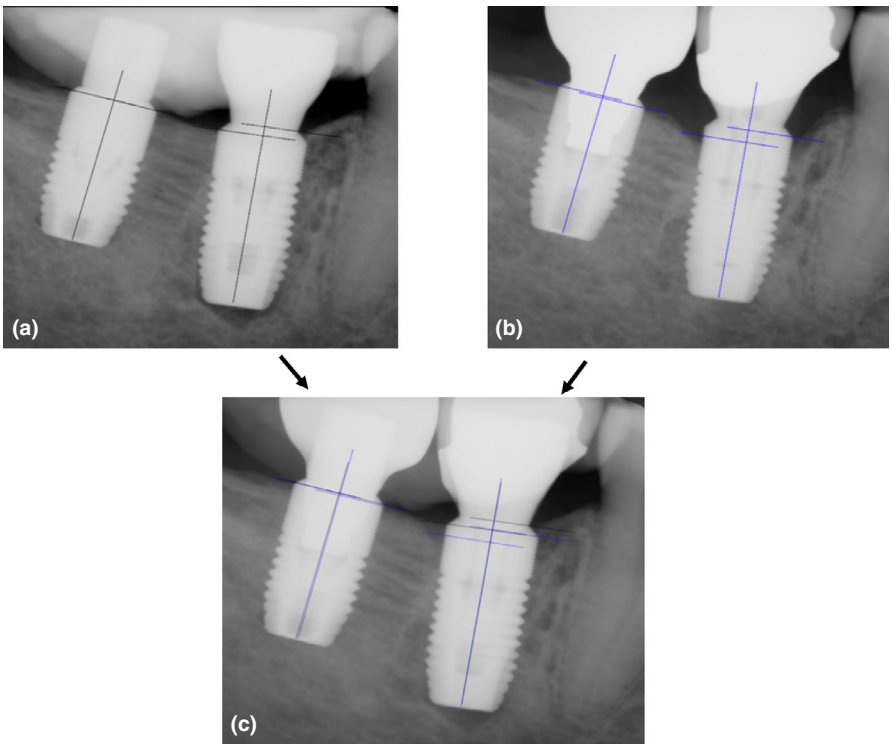

FIGURE 1 (a) Baseline measurements on standardized radiographs; (b) measurements after one year; (c) superimposed measurements to calculate peri-implant crestal bone change

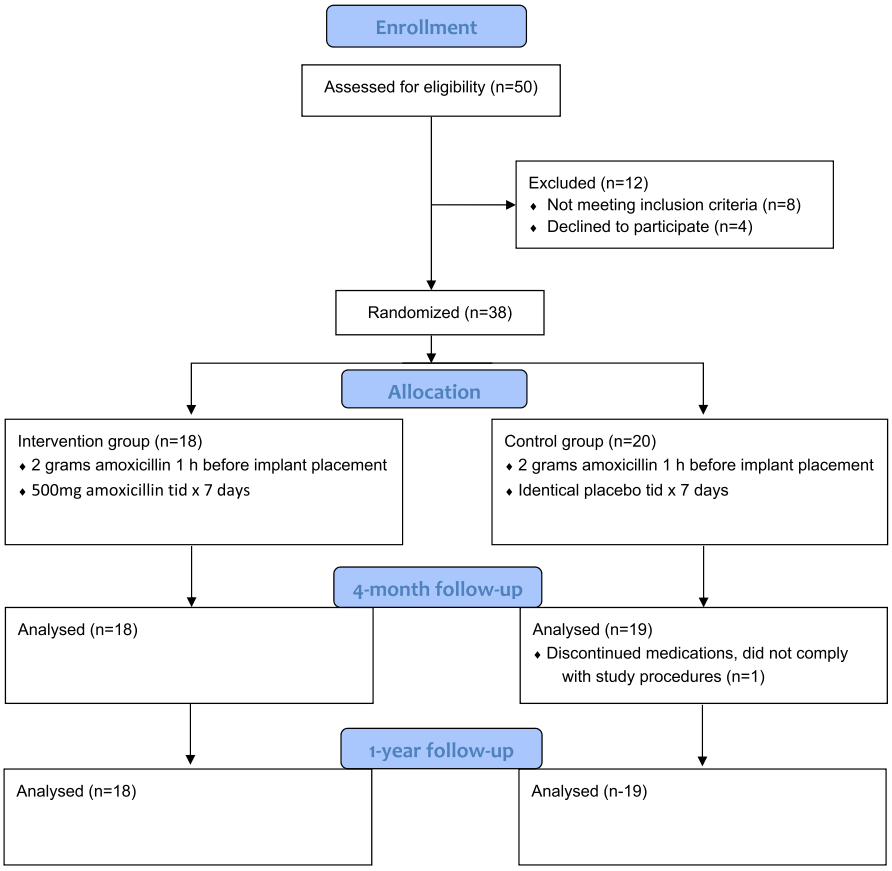

FIGURE 2 CONSORT flow diagram

was assessed using the handles of two blunt instruments (Smith & Zarb, 1989), and the presence or absence of any symptoms related to infection, inflammation or neuropathy was recorded. At the one-year examination, peri-implant probing depth was evaluated as well. One calibrated examiner performed all radiographic measurements (SM), and another examiner performed the clinical evaluations (IK). Intraclass correlation coefficient (ICC, two-way mixed-effect model) assessed intra-examiner reliability of the crestal bone-level change. The reliability was excellent, with an intra-examiner ICC>0.90.

2.4 | Statistical methods

To obtain a statistical power of 80% to reject the null hypothesis of an absence of any differences between groups in crestal bone-level change when the population mean difference is 0.5 mm at an alpha level of 5%, a sample size of 17 participants per group was required (PASS version 12, NCSS). This difference of 0.5 mm is considered to be clinically significant (Bruyn et al., 2013). The normality of data distribution was assessed using the Shapiro–Wilk test. Independent sample t tests, Mann–Whitney *U* and Fisher's exact tests were used to compare groups. A mixed model for repeated measures with time (4 months and 1 year), group and the interaction time*group was utilized for crestal bone-level change. Post hoc comparisons between groups at each time point were then performed to calculate mean differences and their 95% confidence interval. An average value was used when a patient received two implants for crestal bone-level change, mPI and surgical parameters. The implant with the worst outcome was used for swelling, ecchymosis, suppuration and dehiscence. Cohen's d was used to consider effect size for mean peri-implant bone-level change. A Pearson correlation was used to assess the relationship between surgery duration and crestal bone-level changes. SPSS version 24 (IBM Co.) and SAS version 9.4 (SAS Institute Inc.) were used for analyses. A p value ≤.05 was considered statistically significant.

3 | RESULTS

Among the fifty patients who were initially invited to participate in the study, thirty-eight were eligible and accepted to take part. The participants were randomly assigned to either the intervention or control group. One study participant was excluded from the statistical analysis because of non-compliance (Figure 2). This participant did not want to continue to take the antibiotics (or placebo) that we had prescribe him and did not want to continue to participate due to time constraints. Therefore, not enough data were available to do an intent-to-treat analysis for this participant.

Table 2 shows the sociodemographic and medical information of the study group. The mean age of participants was 57.4 ± 11.3 years (mean ± SD), and the groups were homogenous for all characteristics (age, sex, ethnicity, education, current and former smokers, diabetes). Surgical parameters (insertion torque, incision length, bone quality, implant location [maxilla vs. mandible]) and implant characteristics (diameter, length, implant system) were similar for all except two parameters (Table 3). There was a significantly higher proportion of patients having two implants in the control group (52.6%) compared with the intervention group (16.7%, p = .038). In addition, the mean surgery duration was significantly longer in the control group (57.6 ± 21.1min.) compared with the intervention group (43.5 ± 13.2 min., p = .021). Consequently, it was observed that when more implants were placed, the surgery lasted longer (two implants (n = 13): 66.6 ± 17.0 min. vs. one implant (n = 24): 42.1 ± 13.7 min., p < .001). We investigated the effects of surgery duration on crestal bone-level changes with a regression model. Surgery duration had no significant effect on the peri-implant crestal bone change (Pearson's correlation R = .028, R^2 = .0008, p = .871).

TABLE 2 Participants' sociodemographic and medical information

Variables	Intervention (n = 18)	Control (n = 19)
Mean age: (years, ± SD)	55.5 ± 9.1	59.1 ± 13.1
Sex (n, %):		
Female	11 (61.1)	10 (52.6)
Male	7 (38.9)	9 (47.4)
Ethnic background (n,%):		
North America	10 (55.6)	9 (47.4)
Europe	7 (38.9)	7 (36.8)
Other	1 (5.6)	3 (15.8)
Education (n, %):		
University	10 (55.6)	12 (63.2)
College or less	8 (44.4)	7 (36.8)
Currently smoking (n, %):		
Yes	0 (0.0)	1 (5.3)
No	18 (100)	18 (94.7)
Former smoker (n, %):		
Yes	8 (44.4)	9 (47.4)
No	10 (55.6)	10 (52.6)
Diabetes (n, %):		
Yes	1 (5.6)	2 (10.5)
No	17 (94.4)	17 (89.5)

Table 4 shows the mean radiographic peri-implant crestal bone changes between groups. In the intervention group, the mean combined crestal bone change was −0.44 ± 0.43mm while it was −0.27 ± 0.56mm for the control group after 1 year. The difference between groups (intervention–control) for mean combined crestal bone-level changes was −0.17 mm (95% CI −0.46, 0.13). The overall difference between groups was not statistically significant (p = 0.533), neither were the effect of time (p = .690) or their interaction (p = .196). Cohen's d was 0.008 after 4 months and 0.337 after 1 year. A frequency distribution analysis revealed that in the intervention group, seven subjects had >0.5 mm and <1 mm and 1 subject had >1 mm of crestal bone loss. In the control group, six subjects had >0.5 mm and <1 mm and 2 subjects had >1 mm of crestal bone loss. No participant in either group had >2 mm of peri-implant bone loss.

Figure 3 shows the participants' perceived pain during the first seven days after surgery. The perceived pain intensity was overall mild (VAS score = 10–30) in both groups. The median pain intensity for both the control and intervention groups reached a peak 24 h after the surgery (Figure 3). There was no perceived pain after the morning of the fourth day in the intervention group, and the pain intensity was the same for the remainder of the postoperative healing period

(Figure 3). In the control group, the perceived pain reached the 'zero' value after the morning of the 7th day. On several occasions during the first seven postoperative days, the median pain score was 2 in the control group while it was 0 in the intervention group. More specifically, this difference was statistically significant on the fourth day at noon ($p = .047$) and at night ($p = .036$) and on the 5th day at night ($p = .036$). The mean number of supplemental analgesics taken by the participants in the intervention group was 1.5 ± 4.5 tablets, and for those in the placebo group, it was 1.0 ± 2.8 tablets. This difference was not statistically significant between the two groups. Regarding interferences with daily activities for the first seven postoperative days, sporadic significant differences were seen between the groups. Participants in the control group experienced more difficulty in opening their mouth, and more interference with sleep, work, school, social and recreational activities compared with the intervention group and these parameters were significantly worse at few specific time points during the initial postoperative period.

There were no significant differences in short-term (one- and three-week follow-ups) or mid-term (four-month and one-year follow-ups) postoperative morbidities between the two groups. Postoperative morbidities were scarce. Two participants in the intervention group had suppuration at the one-week examination and were asked to rinse with 0.12% chlorhexidine gluconate bid for two weeks. At the three-week follow-up, there was no more suppuration and peri-implant tissues were clinically healthy. At the four-month examination, another patient in the intervention group had a gingival abscess with suppuration around her implant that was caused by food impaction in the area. Peri-implant debridement under local anaesthesia was provided and the abscess subsided four weeks later. No antibiotics were used in both cases.

The implant survival rate was 100% at the 1-year follow-up in both groups, with all implants loaded for at least six months and peri-implant probing depth ≤5 mm in all sites with clinically healthy peri-implant tissues. The only participant who reported side effects was in the placebo group and experienced an episode of diarrhoea two days after implant placement.

TABLE 3 Surgical parameters and implant characteristics

Variables	Intervention ($n = 18$)	Control ($n = 19$)
Patients having (*n*, %):		
One implant	15 (83.3)	9 (47.4)
Two implants	3 (16.7)	10 (52.6)
Mean implant diameter (mm, ±SD)	4.65 ± 0.64	4.48 ± 0.62
Mean implant length (mm, ±SD)	10.28 ± 1.53	10.47 ± 1.17
Mean insertion torque (Ncm, ±SD)	39.72 ± 8.99	41.32 ± 6.15
Mean surgery duration (min, ±SD)	43.5 ± 13.2	57.6 ± 21.1
Mean surgical incision length (mm, ±SD)	20.0 ± 6.6	22.5 ± 6.7
Mean bone quality (category, ±SD)	2.6 ± 0.5	2.42 ± 0.8
Implant location (*n*, %):		
Maxilla	9 (50.0)	9 (47.4)
Mandible	9 (50.0)	10 (52.6)
Implant system (*n*, %):		
Astra Tech TX™	9 (50.0)	9 (47.4)
Astra Tech EV™	9 (50.0)	10 (52.6)

4 | DISCUSSION

To our knowledge, this study was the first placebo-controlled double-blinded randomized clinical trial simultaneously studying the effects of postoperative antibiotics on radiographic, clinical and patient-based outcomes after implant surgery. The addition of a 7 day postoperative regimen of amoxicillin did not provide significant effects on peri-implant crestal bone remodelling, morbidities and implant survival, one year after placing straightforward platform-switched implants in healthy patients. This type of study design was aimed at reducing as much as possible the risk of bias and increasing the quality of the evidence.

The Dental Implant Clinical Research Group study included 1,762 implants placed in individuals from several Department of Veterans Affairs Medical Centres and University Research Clinics (Manz, 2000). The authors observed that a postoperative intake of antibiotics was associated with a slightly greater bone loss up to six months after implant placement, but no randomization according to antibiotic use was done. Importantly, the decision whether to prescribe perioperative antibiotics was left to the surgeon and it was most likely influenced by the surgery's complexity and the patient's systemic condition. This lack of randomization could contribute to selection bias, which could explain further peri-implant bone loss rather than the postoperative antibiotic regimen itself. However, our worst scenario, that is, a longer intervention with higher number of implants (2 *vs* 1), showed that the peri-implant bone loss was not associated with the surgery's complexity.

TABLE 4 Peri-implant crestal bone-level changes

Peri-implant bone change (mean (SD))	Intervention	Control	Mean difference† (95% CI)	Time *p* value	Group *p* value	Time*Group *p* value
4 months (mm)	−0.38 (0.41)	−0.38 (0.35)	0.00 (−0.29, 0.30)	.690	.533	.196
1 year (mm)	−0.44 (0.43)	−0.27 (0.56)	−0.17 (−0.46, 0.13)			

†Intervention−control. 95% CI and *p* values are from a mixed model for repeated measures.

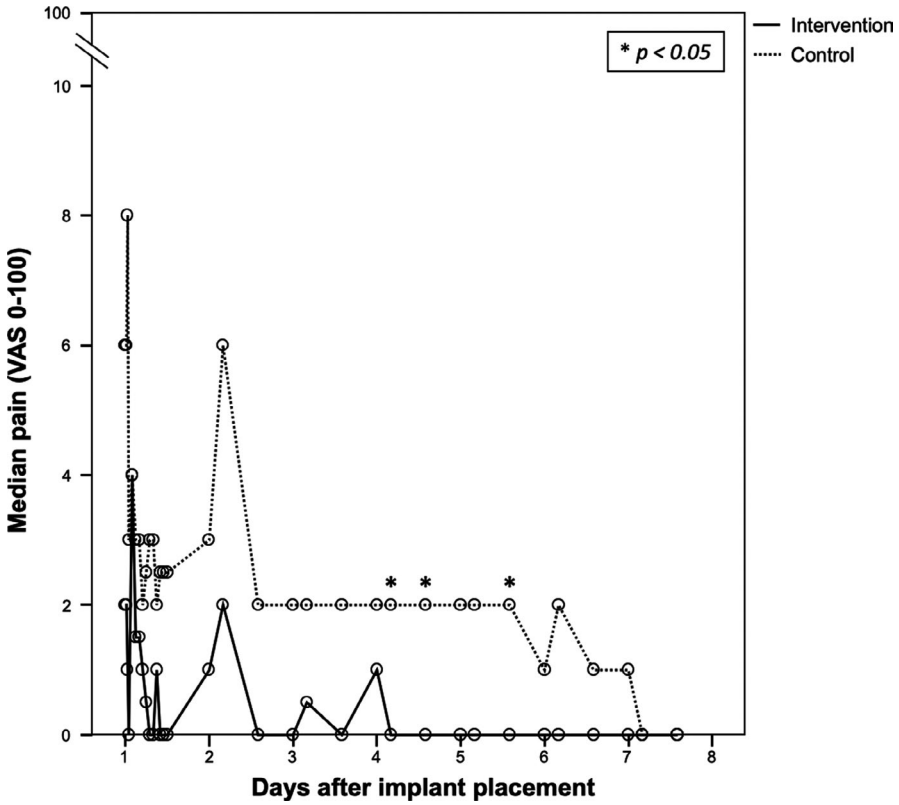

FIGURE 3 Patient's pain experience within 7 days after implant placement

The absence of a statistically significant difference in the mean peri-implant crestal bone change may be explained by several factors. First, platform-switched implants have shown minimal bone remodelling compared to implants with regular platforms (Hsu et al., 2017). Our findings are well within the range observed in a systematic review around implants with internal connections where peri-implant crestal bone loss varied between 0.07 and 0.87 mm (de Medeiros et al., 2016). Furthermore, the surgeons involved in this study had a minimum of 10 years of experience and performed the implant surgeries under standardized conditions in order to minimize performance bias. Indeed, surgeon's years of experience and skill level are associated with a decrease in early implant failure rate (Antoun et al., 2017). Finally, the observed effect size (Cohen's d = 0.34) was smaller than expected when the sample size calculation was performed (Cohen's d = 1.00). It should be remarked that the observed standard deviation (pooled SD = 0.5) was the same as expected when doing sample size estimation. Therefore, the sample size would have provided a statistical power of 0.80 if the difference between groups would have reached the clinically significant threshold of 0.5 mm.

There were no significant differences in postoperative morbidities and implant survival rates between the intervention and placebo groups. Similar results have been observed by other studies comparing pre- *vs* pre- and postoperative antibiotics in implantology (Arduino et al., 2015; Binahmed et al., 2005; Caiazzo et al., 2011; El-Kholey, 2014; Tan et al., 2014). In one study, only those patients who had not taken any perioperative antibiotics did not achieve complete wound closure at the fourth postoperative week (Tan et al., 2014). The necessity of giving antibiotics before, at the time of or after implant placement to improve the implant survival rate was questioned in straightforward implant surgeries, which characterized their patient population as well as ours. While it has been shown that the use of peri-operative antibiotics reduced the risk of implant loss by 2%, our data do not suggest that it provides any benefit for uncomplicated implant surgery in healthy patients. However, a beneficial effect in uncomplicated cases cannot be excluded (Lund et al., 2015). One must keep in mind that it is not always possible to determine ahead of time if the implant surgery will be complex or not, even when the patient is healthy. Moreover, several etiological factors unrelated to the patient's health or the surgery's complexity have been associated with increased risk of implant failure: poor bone quantity and quality, placement of implant in the maxilla and in posterior regions of the jaws, shorter implants, lack of initial stability, low insertion torque of immediately or early loaded implants, and lack of surgical experience (Chrcanovic et al., 2014, 2016). According to the latest studies, a single preoperative antibiotic regimen seems to represent the most efficient option to reduce implant failure rate while limiting antibiotic exposure (Kim et al., 2020).

Participants taking the postoperative placebo experienced significantly more pain severity compared with the intervention group on the fourth and fifth days after surgery. Notably, implant surgeries lasted significantly longer in the control group. This could explain the difference between groups because postoperative pain has been shown to significantly correlate with implant surgery duration (Kuroi et al., 2015; Mei et al., 2016). Another important factor that might have played a role in the increased pain severity experienced in the control group was the significantly higher number of implants inserted compared with the intervention group. Patients having a

larger surgical site were found to be more susceptible to experience severe pain (Mei et al., 2016). Nevertheless, the overall median pain severity observed in both groups during the first seven days after surgery was considered mild. This finding was observed in other studies performed under similar conditions where an experienced surgeon placed a single implant without the use of bone grafting procedures (Eli et al., 2003; Hashem et al., 2006; Tan et al., 2014). In this study, the median implant surgery duration in both groups was less than an hour and all participants were told to take analgesics for the first 48 h after surgery, which could explain the low postoperative pain severity reported. This underlines the importance of monitoring medication intake during the postoperative healing period to eliminate confounding factors.

The control group also experienced significantly more interference with daily activities seven days after surgery compared with the intervention group. One might expect this difference since pain severity was higher among these participants. Pain is a major life-affecting factor influencing quality of life. More specifically, interference with sleep was significantly higher from the third to the sixth postoperative day in the control group. On the seventh day, the difference was no longer significant. This decline was consistent with the decreased in pain severity that was not significantly different between the two groups. It was reported that participants experiencing higher pain severity and interference with daily activities two and seven days after surgery were more susceptible to experience implant failure subsequently (Nolan et al., 2014). All five failures in their study occurred in participants who did not take preoperative antibiotics. We did not find this association, most likely due to our study's small sample size, experienced surgeons and preoperative antibiotics given to all participants. Although only one participant reported side effects (diarrhoea) in the placebo group, this result should be interpreted cautiously since adverse events were self-reported at the follow-up appointment and not collected on a daily basis, possibly introducing a recall bias.

Since our study population was healthy, and the implant surgeries did not involve additional bone grafting procedures, the results cannot be generalized to other populations such as smokers, bruxers, medically compromised and more complex surgeries and implant surgeries executed by inexperienced surgeons. The small sample size precludes any generalization for larger populations and prevented us from accurately determining an implant survival rate for either group. Another limitation of this study was that the frequency of use of the 0.12% chlorhexidine mouthwash was not logged in the participants' daily diaries. It was shown in a large clinical study that the perioperative use of a 0.12% chlorhexidine gluconate mouth rinse could significantly minimize the incidence of postoperative implant complications (Lambert et al., 1997). Postoperative chlorhexidine mouthwash use should therefore be monitored in future investigations. Lastly, there were a higher number of participants receiving two implants in the placebo and this was due to an unequal distribution despite using random allocation.

5 | CONCLUSIONS

Giving systemic postoperative antibiotics after implant placement did not influence peri-implant crestal bone change and postoperative morbidities. A single preoperative dose of antibiotics one hour prior to implant placement may be sufficient to prevent implant complications since this will minimize risk of developing antibacterial resistance compared with an additional postoperative antibiotic regimen. This will have to be confirmed in larger controlled trials.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

AUTHOR CONTRIBUTIONS

Robert Durand: Conceptualization (lead); Data curation (equal); Formal analysis (equal); Funding acquisition (lead); Investigation (lead); Methodology (lead); Project administration (lead); Resources (lead); Software (lead); Supervision (lead); Validation (lead); Visualization (equal); Writing-original draft (lead); Writing-review & editing (lead). **Issam Kersheh:** Conceptualization (supporting); Data curation (lead); Formal analysis (supporting); Funding acquisition (supporting); Investigation (equal); Methodology (equal); Project administration (equal); Resources (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **Stéphanie Marcotte:** Data curation (lead); Formal analysis (supporting); Investigation (equal); Methodology (supporting); Writing-original draft (equal); Writing-review & editing (equal). **Pierre Boudrias:** Data curation (equal); Investigation (equal); Project administration (equal); Resources (equal); Supervision (equal); Writing-original draft (equal); Writing-review & editing (equal). **Matthieu Schmittbuhl:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Project administration (supporting); Resources (equal); Software (equal); Supervision (supporting); Validation (equal); Writing-original draft (equal); Writing-review & editing (equal). **René Voyer:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Resources (equal); Software (equal); Supervision (supporting); Validation (equal); Writing-original draft (equal); Writing-review & editing (equal).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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