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Comparison between two different antibiotic regimens for the placement of dental implants: A phase-I randomized clinical trial

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This thesis entitled:

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Was evaluated by a jury composed of the following members:

Dr. Elham Emami, President of the jury

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Résumé

Introduction : Afin de minimiser la morbidité postopératoire après une chirurgie implantaire, plusieurs régimes d'antibiotiques péri-opératoires ont été suggérés, mais leurs effets sur le remodelage osseux péri-implantaire n'a pas été clairement établi. De plus, l'utilisation répandue des antibiotiques en médecine dentaire et en médecine est remise en question étant donné l'émergence récente des résistances bactériennes aux antibiotiques.

Objectifs : L'objectif primaire de cette étude pilote était de produire des données préliminaires et d'évaluer si des doses postopératoires d'antibiotiques après la pose d'implant prises sur sept jours influenceraient les niveaux osseux péri-implantaires après 4 mois chez les patients en santé subissant la pose simple d'un implant de type « platform-switching ». Les objectifs secondaires étaient d'évaluer la sévérité de la douleur, la morbidité postopératoire, et le taux de survie après un an.

Méthodes : Trente-huit participants ont été recrutés dans un essai clinique parallèle randomisé à double insu. Les participants du groupe intervention ont reçu 2 g d'amoxicilline une heure avant la chirurgie implantaire, et un régime postopératoire de 500 mg d'amoxicilline d'une durée de sept jours. Les participants du groupe contrôle ont pris seulement une dose de 2 g d'amoxicilline une heure avant la chirurgie et un placébo postopératoire. Les changements du niveau osseux péri-implantaire mésial et distal (résultat primaire) ont été mesurés à la pose de l'implant et quatre mois plus tard à l'aide de radiographies rétroalvéolaires standardisées. La sévérité de la douleur et les morbidités postopératoires (résultats secondaires) ont été évaluées à l'aide d'examens cliniques et de questionnaires auto-administrés. Le taux de survie implantaire a été évalué un an plus tard. Des analyses bivariées et descriptives ont été utilisées

pour analyser les données. Une valeur de $P \leq 0.05$ a été considérée statistiquement significative.

Résultats : Trente-sept participants ont complété l'étude (âge moyen : 57,4 ± 11,3 ans). Les changements moyens du niveau osseux péri-implantaire combiné pour le groupe intervention et le groupe contrôle étaient respectivement de -0.29±0.36mm et de -0.11±0.35mm. Les différences entre les groupes pour le changement moyen du niveau osseux péri-implantaire combiné et la sévérité de la douleur n'étaient pas statistiquement significatives ($P> 0.05$). Les interférences avec les activités quotidiennes étaient parfois significativement plus importantes pour le groupe contrôle comparativement au groupe intervention ($p< 0.05$), dépendamment du critère évalué et du nombre de jours écoulés depuis la chirurgie. Le taux de survie implantaire était de 100 % dans les deux groupes après un an.

Conclusions : Les résultats de cette étude pilote suggèrent qu'un régime postopératoire d'antibiotiques chez les patients en santé subissant la pose simple d'implant de type « platform-switching » n'est pas nécessaire. Des investigations additionnelles sont nécessaires afin de confirmer les résultats de cette étude pilote.

Mots-clés : Implant, antibiotique, placébo, os crestal, douleur, étude de phase I

Abstract

Introduction: In order to minimize postoperative morbidity and failure of dental implant therapy, several antibiotic regimens have been proposed in the literature. However, the extensive use of antibiotics in health care has been debated due to adverse effects and bacterial resistance. Furthermore, the impact of postoperative antibiotics on peri-implant bone level is still not clear.

Objectives: The primary objective of this pilot study was to produce preliminary data and to assess whether giving postoperative antibiotics after implant placement over seven days would influence peri-implant crestal bone levels after four months in healthy patients undergoing platform-switched implant placement. The secondary objectives were to evaluate postoperative pain severity, surgery-associated morbidities, and one-year implant survival rate.

Methods: Thirty-eight individuals were enrolled in a double-masked two-arm randomized clinical trial. Participants in the intervention group received 2 g of amoxicillin one hour before implant placement followed by a seven-day post-operative course of 500 mg of amoxicillin. Participants in the control group took only 2 g of amoxicillin before surgery and an identical placebo postoperatively. The changes in mesial and distal crestal bone level (primary outcome) were measured at baseline and four-month follow-up using standardized periapical radiographs. Pain severity and surgery-associated morbidities (secondary outcomes) were evaluated by clinical examinations and self-administered questionnaires. Implant survival rate was assessed at the one-year follow-up. Descriptive and bivariate analyses were used to analyze the data. A P value ≤ 0.05 was considered statistically significant.

Results: Thirty-seven participants completed the study (mean age: 57.4 ± 11.3 years). The mean combined peri-implant crestal bone level change for the intervention and control group was -0.29±0.36mm and -0.11±0.35mm, respectively (n=37 participants). The differences between groups for mean combined crestal bone level change and pain severity were not statistically significant (P> 0.05). Interferences with daily activities were sometimes significantly more important for the control group compared to the intervention group (P< 0.05), depending on the criteria and on the number of days elapsed since the surgery. The implant survival rate was 100% in both groups after one year.

Conclusions: Results from this study suggest that an additional postoperative intake of antibiotics in healthy patients undergoing straightforward platform-switched implant placement might not be necessary. Further investigations are needed to confirm these pilot study findings.

Keywords: Implant, antibiotic, placebo, crestal bone, pain, phase-I trial

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LIST OF SYMBOLS AND ABBREVIATIONS

Vs	Versus
SLA®	Sand-blasted, large-grit, acid-etched
I kB	Inhibitor of nuclear factor kappa-B
%	Percentage
mm	Millimeter
ICOI	International Congress of Oral Implantologists
CBCT	Cone Beam Computed Tomography
DAS	Dental Anxiety Scale
VAS	Visual analog scale
EMA	Ecological Momentary Assessment
PC	Personal computer
E. coli	*Escherichia coli*
C. difficile	*Clostridium difficile*
g	Gram
mg	Milligram
NNT	Number Needed to Treat
AMSTAR	A Measurement Tool to Assess Systematic Reviews
mPI	Modified Plaque Index
CRCHUM	Centre de recherche du Centre hospitalier de l'Université de Montréal
µg	Microgram
ALP	Alkaline phosphastase

DEDICATION

To my father's spirit
To my beloved family and friends

To all who have supported me through hard times

Thank you Chaza, Majd, Joyce, Marie Rose, Salem, Munif, Faheem, Aminah for being a source of love, support and encouragement.

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CHAPTER I

LITERATURE REVIEW

1.1 INTRODUCTION

No one can deny the importance of antibiotics in medicine and dentistry. However, misuse or overuse of antimicrobial medications may have detrimental effects on one's health. Indeed, widespread usage of antibiotics increases the risk of developing antibiotic-resistant bacteria strains (1, 2), specifically, the community-acquired species, which has been observed over the past two decades (3, 4).

The population's demand for dental implants has been increasing due to their high survival rate and their significant improvements of a patient's quality of life. On the other hand, failures have been reported and bacterial infections are thought to play an important role (5). Clinical studies have shown conflicting results regarding the effect of perioperative use of antibiotics on implant survival rate, while their consumption may cause adverse consequences (6, 7). However, other studies have proven that the benefits outweigh the risks of secondary effects (8). Different prophylactic regimens can be found in the literature in order to increase the survival rate of dental implants by reducing the risk of infection (8, 9). Two recent meta-analyses of randomized clinical trials comparing patients with implants who received antibiotics pre- and/or post-operatively to those who did not take any antibiotics, have shown that in the latter group, there were statistically significant higher implant failures (10, 11). The authors of the latest Cochrane review concluded that preoperative antibiotics given one hour before implant placement surgery significantly reduced implant failure rates (9). However, the

authors could not assess whether it was beneficial to give postoperative antibiotics in addition to a preoperative intake or as a sole antibiotic regimen. Consequently, in order to prevent the overuse of antibiotics and the potential emergence of drug resistant bacteria, it would be advisable to find an optimal protocol including minimal antibiotic exposure while maintaining an acceptable implant survival rate. In addition, investigators have found that patients who were taking antibiotics postoperatively have shown less peri-implant crestal bone loss after six months of implant placement compared to individuals who did not receive any post-operative antibiotics (12). However, there is very little data available on the influence of antibiotics on the crestal bone level change.

Subjective outcomes after implant placement are poorly documented in the literature. Indeed, patients' pain and discomfort have not been taken into account in most of the dental implant clinical trials and little is known about their prevalence and intensity after surgery, more specifically with regards to different antibiotic regimens (11). Moreover, very few implantology studies have compared the effects of different antibiotic regimens on the implant survival rate including subject-based, clinical, and radiographic outcomes simultaneously. Therefore, the goals of this two-arm double-masked randomized phase-I clinical trial was to evaluate the influence of postoperative antibiotics on peri-implant crestal bone remodeling after four months, postoperative pain and morbidity, and one-year implant survival rate in healthy patients undergoing straightforward platform-switched implant placement.

1.2 OSSEOINTEGRATION IN IMPLANTOLOGY

Osseointegration was first described by Swedish scientist Per-Ingvar Branemark and his coworkers as a direct, structural and functional connection between living bone and the surface of a load-carrying implant (13). The first implant patient was treated in 1965 by Dr. Branemark (14). The initial implant surface was polished and the implant was cylindrical and screw-shaped. In the 1980s, efforts were made by several implant companies to enhance surface energy and accelerate osseointegration in order to increase implant survival rate and improve patient care. Nowadays, most implants remain screw-shaped or tapered, and their surfaces are micro-textured and/or nano-textured to enhance osseointegration. The success of an implant's osseointegration depends on the following factors: biocompatibility of the implant material, macroscopic and microscopic nature of the implant surface, status of the implant bed (non infected) and bone quality, surgical technique, quality of infection control during surgery, condition of the patient's immune system and subsequent prosthetic design.

Histological studies have shown that the osseointegration process is more complex than initially demonstrated, although similar to direct fracture healing (15). The osseointegration process starts with early events beginning within two hours of implant placement. The threads of self-tapping screw-shaped implants usually provide initial mechanical stability. A blood clot is formed around the implant, serving as a matrix for neoangiogenesis, extracellular matrix deposition, and bone forming cells (16, 17). Bone remodeling occurs within one week of implant placement. It starts with contact osteogenesis, where osteogenic cells migrate directly onto the implant surface and generate the bone matrix (16). This phenomenon has only been observed on textured implant surfaces. Fourteen days later, the woven bone

formation is more pronounced. Most of this bone formation starts at a distance from the implant, from the borders of the drill hole, and is thus called “distant osteogenesis”, where osteoblasts migrate to the surface of the implant cavity, differentiating and stimulating new bone formation. Osteoclasts play a role in bone resorption, especially in the zones where there is implant pressure in the osteotomy site. After two to three weeks, the implant’s stability is at its lowest because of the smaller percentage of mature mineralized bone matrix in contact with the implant as a result of the remodeling process. Four weeks after implant placement, the newly formed bone extends and covers most of the implant walls. At six to twelve weeks of healing, mineralized bone fills all the remaining space between the implant and the native bone. At that point, secondary implant stability is at its highest, increasing only slightly thereafter. Its strength depends largely on new bone formation at the bone-to-implant interface (18).

Recent human and animal studies have shown that roughened sandblasted and acid-etched implants showed a better bone-to-implant contact compared to implants with a polished surface. This observation was noted as early as one week after implant placement. A limited number of human studies have shown healing with screw-type sandblasted acid-etched dental implants (SLA®, Straumann AG, Basel, Switzerland) (19-22). The findings from these studies indicated an average bone-to-implant contact of 22% of the total implant surface in SLA® and SLActive® (Straumann AG, Basel, Switzerland) implants at the end of the first week, which consisted mainly of native bone. This number went up to 28% at the end of the second week, and new bone covered 12.2% and 14.8% of the surface in SLA® and SLActive® implants respectively. At four weeks, the old bone covered 28.3% and 13.9% of SLA® and SLActive®

implant surfaces respectively, and the new bone covered 32.4% and 48.3% of SLA® and SLActive® implant surfaces. At six weeks, the percentage of the old bone being in contact with the titanium implants decreased to between 8 and 13.6%, and the new bone covered 61.5% of the surface for both types of implants.

The molecular mechanisms involved in the osseointegration process were not well understood until recently. Major signalling pathways such as IkB kinase/nuclear factor KappaB, start early during osseointegration and subsequently decrease over time (23). Those pathways provide areas of interest that might be modified to enhance osseointegration. Other molecular mechanisms also playing an important role are inflammation, angiogenesis, neurogenesis and skeletogenesis. A human study using whole-genome transcriptional analysis described the principal molecular mechanisms during the first two weeks of the osseointegration process (20, 21).

It was shown that immuno-inflammatory genes were expressed early during the osseointegration process and down-regulated over time. However, their role is not fully understood. For example, enhanced macrophage cytokine expression suggests that modified implant surfaces may accelerate osseointegration as macrophage cytokines are well known to play a part in the inflammatory process after injury, eventually leading the healing process. Further investigation is needed to fully understand their exact role as well as the integration mechanism in dental implants.

During the osteogenesis phase, osteoblast differentiation, ossification and biomineral formation was observed. In human patients, most of these events occur in the first two weeks of osseointegration. Of interest is the period between day four and seven when the embryonic skeletogenesis-associated genes are differentially regulated. The importance of angiogenesis is another area where osseointegration can be targeted for modification since blood vessels provide a network and direct access to the bone-implant interface for growth factors and bone forming cells such as osteoblasts. A very prominent over-expression of genes associated with neurogenesis was observed during the early stages of osseointegration, though their role is unclear. Neuropeptide Y is one molecule that was shown to modulate osteoblast function.

The capacity of micro-textured implant surfaces to enhance and accelerate gene expression of bone matrix molecules and surface hydrophilicity increases osteogenesis and angiogenesis. This finding provides new avenues in implant surface modification and development. Newer implant designs do indeed incorporate such surface modifications in order to enhance the implant survival rate and accelerate the osseointegration process. Nevertheless, little has been done in clinical research regarding potential biochemical or pharmacological methods to accelerate the osseointegration process.

1.3 EVALUATION OF DENTAL IMPLANT OUTCOMES

1.3.1 Criteria to determine implant success

The success of a dental implant may be subjective and depends on both the surgeon's and the patient's perceptions. Clinical, radiographic and patient-based outcomes have been used since

the 1980s. On the other hand, dental technologies and dental implant designs have significantly changed since then, and implant success criteria have evolved over the years. More importantly, implant success is not synonymous with implant survival. Implant success is characterized by specific preselected criteria that are met, while implant survival simply means that the implant remains *in situ* or in function without any other criterion being considered. It must be measured once the implant's osseointegration is completed and the implant is restored, which usually takes between two and six months. The ten-year cumulative implant survival rate has recently been reported in a systematic review to be around 95% (24). The success rate of implants may greatly vary depending on the outcomes measured. Several success criteria have been proposed by different groups of experts. The original criteria for implant success were described by Albrektsson and colleagues (25) and included the following:

1) The individual, unattached implant should be immobile when tested clinically;

2) No radiographical evidence of peri-implant radiolucency;

3) Less than 0.2mm annually of vertical bone loss after first year of service;

4) Absence of persistent pain, infection, neuropathies, paresthesia or violation of mandibular canal.

5) Based on these criteria, a success rate of 85% at the end of a five-year observation period and 80% at the end of a ten-year period were minimum levels for success at that time.

It is important to note that these success rate thresholds were measured with the original Branemark® polished-surface implants. It was determined that the mean crestal bone loss for

Branemark® osseointegrated implants was 1.5 mm for the first year followed by a mean crestal bone loss of 0.1 mm/year (26). Thus, a mean bone loss threshold of 0.2 mm per year after the first year in function was accepted as a criterion for success. Three years later, an additional criterion for success was added to take into account the implant restoration aesthetic appearance:

> 6) The implant design does not preclude placement of a prosthesis or crown with an aesthetic appearance that is satisfactory to the patient and dentist (27).

A consensus report was published later on using the same success criteria but removing the expected success rate and radiographical peri-implant radiolucency (28). The authors emphasized the importance of using standardized radiographs to measure crestal bone loss with predetermined reference points and angulations.

With the advent of implant surface texturing methods, Buser and colleagues studied soft and hard tissue integration around Straumann® rough-surface implants after one year using several clinical parameters to determine implant success: plaque index, sulcus bleeding index, probing depth, distance between implant shoulder and mucosal margin, attachment level, width of keratinized mucosa, and mobility (29). Standardized radiographs were also taken to measure the distance between the implant shoulder and the first visible bone contact. The authors used the following success criteria:

1) Absence of persistent subjective complaints, such as pain, foreign body sensation and/or dysesthesia;
2) Absence of a recurrent peri-implant infection with suppuration;
3) Absence of mobility;

4) Absence of a continuous radiolucency around the implant;

5) Possibility for restoration.

Furthermore, the authors classified implant failures as early or late failures. Early failures occur during the first five months following implant placement. Overheating of the bone during drilling procedures, lack of primary stability of the implant, masticatory loading forces, and/or bacterial contamination during surgery may contribute to implant failures. Late failures occur during the maintenance phase after successful osseointegration. The clinical signs and symptoms were pain, bleeding on probing, peri-implant suppuration, and increased probing depth. Upon analyzing the data of 100 consecutively placed implants by one surgeon, 98 implants were considered to be successful, while osseointegration was not achieved in one implant, and a peri-implant infection developed in another one, for a success rate of 98% after one year (29).

In an effort to develop a more comprehensive classification system for implant success, The International Congress of Oral Implantologists (ICOI) held a Consensus Conference in 2007 to update implant success criteria and health status based on an Implant Quality Health Scale using four categories based on the original James-Misch Health Scale (30, 31). Implant success, survival and failure were defined based on the following clinical and radiological parameters such as pain, mobility, crestal bone loss, probing depths, and peri-implant disease as presented in Table 1 (32).

Table 1: Health Scale for Dental Implants

Implant Quality Scale Group	Clinical Conditions
Success	a) No pain or tenderness upon function b) No mobility c) < 2 mm radiographic bone loss from initial surgery d) No exudates history
Satisfactory survival	a) No pain upon function b) No mobility c) 2–4 mm radiographic bone loss d) No exudates history
Compromised survival	a) May have sensitivity on function b) No mobility c) Radiographic bone loss > 4 mm (less than half of the implant's body) d) Probing depth > 7 mm e) May have exudates history
Failure	a) Pain upon function b) Mobility c) Radiographic bone loss of more than half the length of the implant d) Uncontrolled exudate e) No longer in mouth

Although the Albrektsson (25) and Buser (29) implant success criteria remain the most commonly used, a lack of international consensus still reigns. This is illustrated by the fact that several authors have used their own criteria for implant success in recent years (33-35). During the 8th European Workshop in Periodontology held in 2012, several working groups were organized to assess the quality of reporting of clinical research in implant dentistry (36). The consensus report identified three main outcome domains that should be included in future implantology studies: patient-reported outcome measures, peri-implant tissue health, and performance of implant supported restorations. More specifically, health-related quality of life, satisfaction, marginal bone level, tissue inflammation, probing depth, longevity and functionality of the implant-supported restoration as well as technical complications were among the outcomes that should be collected in prospective implantology clinical trials.

1.3.2 Bone remodeling around dental implants

Crestal bone loss around implants is a key parameter affecting implant success (37). The marginal bone around the implant crestal region is a major indicator of implant health and its preservation will affect the long term and predictable success of an implant (38). The level of the crestal bone may be measured from the crestal position of the implant at the initial implant surgery. Initial peri-implant bone remodeling occurs as soon as the implant is connected with a healing or prosthetic abutment as a result of establishing a peri-implant attachment called "biologic width" and may take a few months (39). The key factors that may affect initial peri-implant bone remodeling include implant surface texturization and implant platform design (40).

The platform-switching concept was first described in 2006 (41). In this concept, implants with a wider diameter are used with prosthetic abutments of a smaller diameter in order to move the microgap between the prosthetic abutment and the implant platform further away from the crestal bone. Long-term radiographic observations on the use of platform-switched implants have shown less than expected peri-implant crestal bone loss compared to implants restored with prosthetic components of matching diameters. These findings were supported by a systematic review that reported a mean difference of -0.37 mm in peri-implant bone level changes (95% CI: -0.55 to -0.20; P <0.0001) in favour of platform-switched implants (42). Subgroup analyses showed that an implant-abutment diameter difference > or= 0.4 was associated with a reduction in peri-implant bone loss. In recent years, most implant companies have modified their implant design to include the concept of platform-switching to minimize initial peri-implant bone remodeling.

Implant surface texturization has optimized the host-to-implant tissue response by increasing surface area and roughness. In fact, implant surface modifications have led to high implant survival and better predictability, even for more challenging conditions such as immediate implant placement (43) and immediate loading (44-46). In 2009, the proceedings of a consensus meeting of the European Federation of Periodontology regarding the evidence on the effect of the different commercially-available implant surface modifications on marginal bone loss were published (47). The authors concluded that implants with moderately rough surfaces obtained the highest percentage of bone-to-implant contact, that newer generation of surfaces from four of the major world implant companies enhanced bone integration compared to their predecessors, while they could not find any clinically significant evidence that the platform-switched implant design was superior. However, a recent systematic review and meta-analysis has found that the severity of peri-implant bone loss after at least five years in function was significantly less around minimally rough implants compared to moderately rough and rough implants (48). These conflicting results underline the necessity of conducting further well-controlled clinical studies including confounding factors. In fact, time of measurement (38), implant platform location in relation to the crestal bone, soft tissue thickness (49), oral hygiene (50), and smoking habits (51, 52) have been shown to influence bone level changes after the initial healing phase.

The most common method to assess crestal bone remodeling is by radiographic evaluation. There are three types of radiograph that can be used to evaluate peri-implant bone remodeling around an implant: periapical radiographs, orthopantomographs, and cone beam computerized tomography (CBCT). The first two methods are easily accessible and can be performed

quickly and at a low cost, while the latter one is expensive and will expose the patient to a significantly higher radiation dose. Orthopantomographs are mainly inconvenient because they magnify and distort the images, which affects their sharpness compared to periapical radiographs. Investigators have compared periapical radiographs and CBCT to evaluate peri-implant bone levels around implants and have found significant disparities between the two methods (53). A mean difference of 0.47 mm (range: -0.47 to 3.13) was found, indicating that CBCT images underrated the bone level systematically. Hence, intra-oral radiographs should be considered as the standard to monitor the peri-implant bone remodeling over time. Vandeweghe et al. reported that bone remodeling did not undergo significant changes after 15 weeks (54). Other researchers have demonstrated that the median crestal bone loss between the time of implant placement and three months postoperatively was 1 mm (55). When the median crestal bone loss was calculated between three and six months, it was close to zero. A recent systematic review reported a mean marginal bone loss of 1.3 mm over a mean duration of 13.4 years after implant placement (24). Although this value seems insignificant, one must bear in mind that statistical analysis is often patient-based. This might hide the outliers that lost a significant amount of bone, often being represented by a small number of implants. For example, it was found in a long-term study of Branemark implants that the mean bone loss was 0.8 mm after five years, and insignificant changes were reported thereafter (56). However, the prevalence of implants losing more than 3 mm of bone in that study was 5.6% after one year, 10.8% after five years, and 15.2%, 17.2% and 23.5% after 10, 15 and 20 years respectively. Consequently, it is recommended to measure crestal bone changes at both patient- and implant-level in patients with multiple implants to better visualize extreme values and trends over time (57).

Although several risk factors have been identified with peri-implant bone loss, some consider peri-implantitis as the main risk factor while others see crestal bone loss as an unavoidable physiological process following implant placement and loading. While new developments in implant surfaces and design have help minimize peri-implant bone remodeling, very little research has focused on ways to minimize or even prevent peri-implant bone loss using pharmacological or other non-traditional therapies.

1.4 PAIN EXPERIENCE IN IMPLANTOLOGY

Dental implant placement procedures involve surgical trauma to both the soft tissues and the alveolar bone that will result in an acute inflammatory reaction. Swelling is a classic manifestation occurring after surgery and it may trigger pain, loss of function or neural damage (58). Pain intensity has been showed to be low to moderate after dental implant placement and although it decreases over time, it may last up to a week postoperatively (59, 60). The fear of pain might keep a significant portion of patients from seeking implant placement to replace their missing teeth (61). Pain perception after implant placement is influenced by various factors such as previous experiences, stress, the clinical situation, the complexity of surgery, the number of implants, the surgeon's experience, the sex of the patient, the pain experienced earlier and anxiety (62-64).

One of the earliest studies focusing on pain and anxiety related to implant placement was published in 2003 (62). Sixty patients were recruited from a specialist's private practice to participate in the study. Dental anxiety scale (DAS) (65), state anxiety on a visual analog scale

(VAS) and the patient's evaluation of pain on a VAS were collected immediately before and after surgery, and four weeks post-operatively. Significant correlations were found between the subjects' anxiety and pain at different occasions. The best predictor of pain evaluation immediately after surgery and four weeks postoperatively was state anxiety. Another study evaluated pain and anxiety in 18 subjects undergoing implant surgery using several patient-based outcomes (66). The authors found that for the first three days, 27% of patients experienced "lots" or "quite a bit" of interference with chewing, which decreased to 11% by the sixth postoperative day. Swelling was the most frequent symptom reported during the first three days after surgery, dropping from 72% on the first postoperative day to 39% by the sixth day. The mean VAS score for average pain was the highest on the first postoperative day (24/100) and it decreased gradually to 9/100 on the sixth day, 0 representing no pain and 100 being the most intense pain imaginable. Most patients reported some limitations in their daily activities during the first postoperative day with a mean VAS score of 25/100, and this score decreased by half on the second day and gradually decreased further thereafter.

A more recent study including 89 participants investigated pain and anxiety before implant surgery (T0), immediately after surgery (T1), one day (T2), and one week postoperatively (T3) (59). Participants were instructed that VAS scores of 1 to 3 were indicative of mild pain, 4 to 6 moderate pain, and 7 to 10 severe pain, 0 representing "no pain" and 10 "the most intense pain imaginable". The pain score increased from 1.03±0.83 at T1 to 4.13±1.37 at T2, then dropped to 0.98±0.94 at T3. The pain score at T2 was the highest. At T1, 31.4% reported having no pain, while at T2, 33.7% reported mild pain, 62.9% reported moderate pain, and 3.3% reported severe pain. At T3, 39.3% reported having no pain and 60.6% reported mild pain. There was a

significant correlation between the pain score at T2 and the state of anxiety at T1 and T0, and between the pain score at T2 and the state of anxiety at T1 and T2. The authors concluded that anxiety affected pain intensity after implant surgery, corroborating the findings of Eli and colleagues.

Investigators have recently used cellphone-based real-time pain and swelling questionnaires after dental implant surgery (67). In an attempt to boost the validity level of the assessments and increase the number of time point assessments after implant surgery, the authors used a cellular phone-based Ecological Momentary Assessment (EMA) system regulated by a host PC server that automatically sent e-mails to cell phones every two hours on the first day of surgery, and every 24 hours onward until the seventh postoperative day. The outcomes measured were the patient's preoperative anxiety level, postoperative pain and subjective swelling sensation. Subjective intensity of pain and swelling were measured by an 11-grade and a 4-grade rating-scale questionnaire respectively. For the pain level assessment, a score of 0 represented "painless" and a maximum score of 10 indicated "intolerable pain". Regarding swelling sensation assessment, a score of 0 represented "no swelling", a score of 1 meant "swelling of a limited area", a score of 2, "swelling of an extended area", and a score of 3, "swelling extended to an extra-oral region". The data from 25 participants was analyzed. Mean postoperative pain and swelling peaked at six and 36 hours after surgery with a mean rating of 0.87 (0-11) and 1.32 (0-3) respectively. Six risk factors were significantly associated with postoperative pain: presence of diabetes and/or hypertension, duration of surgery, intake of premedication, bone quality, preoperative anxiety and total swelling sensation, while three

were significantly associated with a swelling sensation: accumulated postoperative pain, absence of diabetes and/or hypertension, and bone quality.

Several factors have been shown to influence pain experienced after implant surgery but only a few studies have simultaneously evaluated these potential factors. Although the intensity of pain experienced by individuals undergoing implant surgery has been described as low to moderate, it represents one of the most common barriers keeping patients from seeking dental implant therapy. Controlled clinical trials including the above mentioned factors may shed some light on the extent of the influence operator-based, patient-based and surgery-based factors have on a patient's perceived pain after implant placement.

1.5 THE ROLE OF ANTIBIOTICS IN DENTISTRY

1.5.1 Risks associated with antibiotics overuse

Extensive antibiotic exposure in health care is a well-known risk factor for antibiotic resistance (68). Multidrug-resistant bacteria such as *E. coli* strains have been associated with the overprescription of antibiotics in medicine and dentistry (69). Antibiotics are occasionally associated with many clinical complications ranging from a simple rash to life-threatening superimposed infections. One of the most common and dangerous complications is the *C. difficile* infection. In 2015 alone, about 500,000 Americans suffered from this infection and one out of three patients with this infection was 65 years or older (70). Therefore, proper diagnosis and adequate use in clinical practice are important strategies that will reduce antibiotic exposure (71). In a recent study comparing the side effects of amoxicillin/

clavulanate potassium and clindamycin for the treatment of odontogenic infections, at least 50% of patients who used either antibiotic had at least one side effect ranging from minor complaints such as nausea, abdominal discomfort and diarrhea to elevated liver enzymes, a reaction associated with liver damage (72). The routine use of antibiotics to prevent postoperative complications in oral surgery, especially after dental implant placement, has been subject of much debate in recent years.

1.5.2 Effects of antibiotics on dental implant outcomes

One of the first antibiotic protocols described relating to dental implant surgery was Branemark's protocol (26). One hour before the surgical placement of one or multiple implants, 2 g of phenoxymethylpenicillin was given orally along with a 2% chlorhexidine rinsing solution, and 20 to 25 mg of diazepam *per os* to reduce patient anxiety. Phenoxymethylpenicillin was also given for the first ten postoperative days (2g bid). This protocol was aimed at preventing postoperative infections and increasing chances of osseointegration. However, a recent survey of oral and maxillofacial surgeons in the U.S. has shown different prescription patterns being used for prevention of implant complications (73), underlining a lack of standardization among dental practices. There was no consensus among surgeons regarding perioperative antibiotic regimens for implant placement and their effectiveness at decreasing the implant failure rate. In addition, most of the antibiotic regimens used did not comply with current scientific evidence.

Finland is one of the few countries in the world that has a Dental Implant Registry. A retrospective study was done using non-public information obtained with permission from this registry (74). This study examined a total of 110,543 dental implant placement procedures and

1,038 dental implant removal operations performed between April 1994 and April 2012. The aim of the study was to review the type of antibiotic regimens used for dental implant placement and to analyze the association between antibiotic usage and early implant removal. A total of 61 different antibiotics or combinations of antibiotics were prescribed peri-operatively. Antibiotics were prescribed in 1,640 of the 2,521 (65.1%) implant placement operations. Early implant failure generally occurred within six weeks of implant placement. Its prevalence was 12.7% in those cases where antibiotics were prescribed, and 15% when no antibiotics were prescribed. These differences were not statistically significant. Therefore, the authors concluded that the use of prophylactic antibiotics had little effect on implant complications related to the initial surgery and the success rate.

One of the first major prospective clinical studies investigating the effects of the perioperative use of antibiotics on dental implants success rate was published in 1997 (75). The study included data from 2,973 implants, but the type, timing (pre- *vs* post-op), and duration of the antibiotic treatment were left to the discretion of the surgeon. Follow-up of patients was done for up to three years after the prosthesis was loaded. Higher survival rates were found in patients who had received preoperative antibiotic coverage.

Ten years later, a well-controlled randomized clinical trial investigated the effects of the antibiotics on subjective signs and symptoms after implant placement (76). The study included two groups of 40 patients treated consecutively for a total of 128 implants. In the first group, a pre- and post-operative antibiotic regimen was given. More specifically, participants took 1 g of amoxicillin one hour before the surgery and 2 g during two days. The participants of the

second group were not given any antibiotic coverage. Bacterial samples were taken from the peri-oral skin and a VAS questionnaire was used to evaluate symptoms of infection and inflammation by both the patient and the surgeon. No significant differences were found in the clinical and microbiological parameters between the two groups, although the patient's perception of postoperative discomfort experienced was significantly milder in the antibiotics group.

A multicenter, placebo-controlled, randomized clinical trial included 105 patients recruited from 12 private practices in Spain (77). The goals of the study were to compare the safety and efficacy of 2 g of amoxicillin given one hour prior to dental implant placement with identical placebo tablets given when placing single implants in types II and III bone density. The study participants were divided into two groups. Fifty-two individuals received 2 g of amoxicillin one hour preoperatively, and 53 participants were given identical placebo tablets. Two participants in each group experienced an implant/crown failure, and six participants in each group suffered from a postoperative infection. No adverse events were reported and no statistically significant differences were observed for any of the outcome measures.

Another study had similar results while comparing (78) participants who were given 2 g of amoxicillin one hour preoperatively with participants who were given identical placebo tablets for dental implant placement. The antibiotic group and the placebo group included 254 and 255 participants, respectively. The investigators evaluated the implant and prosthesis failure rates, as well as the presence of adverse events and postoperative complications. Three participants were excluded because they did not complete the study. Four participants in the

group taking antibiotics experienced prosthesis failures versus ten in the group taking a placebo. No adverse events were reported and no significant differences were observed for any of the outcome measures.

Another study including 100 patients undergoing implant placement surgery compared the effects of four different antibiotic regimens on dental implants failure rate (7). Participants in the first antibiotic regimen group were given 2 g of amoxicillin one hour preoperatively and no antibiotics given postoperatively. In the second group, the antibiotic regimen was 2 g of amoxicillin to take one hour preoperatively and 1 g twice a day for seven days following surgery. For the third regimen, participants took 1 g twice a day after surgery for seven days. In the fourth group, no antibiotic regimen was prescribed. Each group included twenty-five participants. They were examined for internal and external oedema, internal and external erythema, pain heat and exudates, as well as implant failure. Two participants in the no antibiotic group had single implant failures versus none in any of the three antibiotic groups. However, this difference was not statistically significant. No infections or side effects were reported.

A double-blind randomized controlled trial evaluated the effects of antibiotic coverage on subjective outcomes such as postoperative morbidity, pain and interference with daily activities, and implant survival rate (79). The 27 participants in the first group were given 3 g of amoxicillin one hour preoperatively and the 28 individuals in the second group were given identical placebo tablets. The surgeons were residents in a specialty program. There was no implant loss in any of the participants of the antibiotic group but five participants from the

placebo group each lost their implant (P= 0.0515). No participant in the antibiotic group presented clear signs of infection versus two participants in the placebo group. Post-operative pain and interference with daily activities were significantly lower in the antibiotic group versus the placebo group at seven days. The authors concluded that the prophylactic use of antibiotics may be beneficial for implant osseointegration and to reduce postoperative pain, especially in cases with longer surgery.

The most recent Cochrane review evaluating the effects of various prophylactic antibiotic regimens *vs* no antibiotics on implant survival rates in patients undergoing dental implant placement was published in 2013 (9). The authors searched several databases up to June 17th, 2013 including the Cochrane Oral Health Group's Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE. The studies included in the review were randomized clinical trials with a follow-up of at least three months. Outcome measures included prosthesis failures, implant failures, postoperative infections and adverse events (gastrointestinal, hypersensitivity, etc.). The data of 1,162 participants from the studies were included in the statistical analyses. The meta-analyses of the six trials showed a statistically significant higher number of participants experiencing implant failures in the groups not receiving antibiotics (RR: 0.33; 95% CI: 0.16 - 0.67, P = 0.002). The number needed to treat (NNT) for one additional beneficial outcome to prevent one person from having an implant failure was 25 (95% CI: 14 - 100), based on an implant failure rate of 6% in participants not receiving antibiotics. There was a borderline statistical significance for prosthesis failures (RR: 0.44; 95% CI: 0.19 - 1.00), with no statistically significant differences for infections (RR: 0.69; 95% CI: 0.36 - 1.35), or adverse events (RR 1; 95% CI: 0.06 -

15.85). The authors concluded that the perioperative use of antibiotics for implant placement is beneficial to improve the implant survival rate, and that taking 2 g or 3g of amoxicillin one hour prior to implant surgery might be recommended. However, the effects of postoperative use of antibiotics could not be determined in this study.

Several randomized clinical trials were published after the latest Cochrane review. The first study was aimed at evaluating the clinical benefits of preventing early dental implant failure by adding a postoperative antibiotic regimen after giving a single dose before dental implant placement (80). Eighty participants were recruited and randomly divided into two groups. The first group received 1 g of amoxicillin before the procedure, and the second group received the same preoperative dose as well as a three-day antibiotic course. Follow-ups were scheduled at three days, seven days and twelve weeks. Pain, swelling, wound dehiscence, and pus formation were assessed. There were no implant failures in either group. The author concluded that a single preoperative antibiotic dose was sufficient to prevent implant failure.

A multicenter randomized controlled clinical trial investigated the effects four different antibiotic regimens on patient-oriented outcomes and postoperative complications after implant placement (81). In this study, 329 healthy adults who had a single tooth edentulous area with sufficient bone width and height for the placement of a dental implant without simultaneous bone grafting were recruited in seven centers located in Singapore, China, Australia, Spain, Taiwan and Iceland. Heavy smokers were excluded from the study. The surgeons and examiners were not made aware of the antibiotic regimen selected, although this was not the case for all participants. Participants were randomly assigned to one of four

treatment groups. The first group took 2 g of amoxicillin one hour before surgery. The second group took 2 g of amoxicillin immediately after surgery. The third group took 2 g of amoxicillin one hour before surgery and 500 mg twice daily on the second and third days after surgery. The fourth group took 2 g of a placebo one hour before surgery. The primary outcomes included patient-reported outcomes such as VAS score on pain, swelling, bruising and bleeding. The secondary outcome variables included clinical recordings of flap closure, pain, swelling, suppuration, and implant stability. Postsurgical complications were assessed at the first, second, fourth, and eighth week postoperatively. There were no significant differences in subject profile among the four treatment groups in terms of age, gender, smoking status, sites of implantation profile, and implant dimensions. No statistically significant differences were found among the four groups regarding pain, swelling, bruising, bleeding, suppuration and implant stability. There was a statistically significant difference between the placebo group and the other three groups when it came to flap closure, where 5% of the participants did not achieve complete flap closure at week four compared to 0% for the other groups. However, at the other time points, there were no significant differences between the groups. The authors concluded that none of the three prophylactic regimens excelled at preventing post-surgical complications or improving patient-reported outcomes.

Another recent multicenter randomized clinical trial evaluated the perioperative use of antibiotics for dental implant placement by comparing the differences between a single dose of amoxicillin given preoperatively and the same dose of amoxicillin given for two additional days postoperatively in patients undergoing conventional dental implants (82). Two dental surgeons in two private practices recruited 360 participants and randomly divided them into

two groups of 180 individuals. Participants in group A received only one dose of amoxicillin preoperatively (2 g) while participants in group B received 2 g of amoxicillin before surgery as well as 1 g of amoxicillin in the evening and 1 g twice a day for two additional days after surgery. Both groups were followed during six months to evaluate the implant failure rate as well as side effects of the antibioprophylaxis. The data from 14 patients in group A and three patients in group B were not available. Two patients in group B experienced a prosthetic failure, losing four implants, while no prosthetic failures were reported in group A. Six patients in group A and four patients in Group B experienced early postoperative complications. However, there were no statistically important differences found between the two groups. As observed by others (80, 81), postoperative antibiotic use was not beneficial to reduce the implant failure rate.

As part of the fourth European Association for Osseointegration Consensus Conference, a complex systematic review was done of the best available scientific evidence regarding the effects on implant survival of the perioperative use of antibiotics during dental implant placement (11). The literature search yielded 846 articles, including ten primary studies and seven systematic reviews that were analyzed as part of the systematic review – two were considered to have a moderate risk of bias and five had a high risk of bias according to the AMSTAR criteria. The two systematic reviews with a moderate risk of bias showed divergent numbers needed to treat (NNT) to prevent one patient from having an implant failure. Four of the primary placebo-controlled studies were included in the meta-analysis. They had a low or moderate risk of bias and the heterogeneity between the studies was low. It was found that preoperative antibiotic use significantly reduced the risk of implant loss by 2% ($P = 0.02$). The

NNT was 50 to prevent one patient from losing an implant. More importantly, none of the primary studies showed that perioperative antibiotics used on their own had any statistically significant benefit. A sub-analysis suggested that in uncomplicated implant placements in healthy patients, using antibiotics was not beneficial to prevent implant loss. On the other hand, the authors concluded that in more complex cases or for medically compromised patients, using antibiotics during dental implant placement could prove to be significantly beneficial.

To date, there have been no randomized clinical trials using a double masked study design including a placebo control given postoperatively to evaluate the potential effects of a postoperative antibiotic regimen in addition to one preoperative dose of antibiotics on simultaneous crestal bone remodeling, postoperative morbidity, implant success rate, clinical outcomes and patient-based outcomes such as pain and interference with daily activities.

CHAPTER II

METHODOLOGY

2.1 OBJECTIVES, HYPOTHESIS

2.1.1 Objectives

The primary objectives of this phase-I clinical trial were:

1- To produce preliminary data and to assess whether giving additional antibiotics after implant placement over seven days would influence peri-implant crestal bone levels after four months in healthy patients undergoing platform-switched implant placement.

The secondary objectives were:

2- To evaluate postoperative pain severity, surgery-associated morbidities, and one-year implant survival rate.

2.1.2 Hypothesis

We tested the following null hypotheses:

1- There is no difference in peri-implant crestal bone loss between healthy patients who received a pre- and postoperative antibiotic regimen compared to those who received only a preoperative dose of antibiotics during surgery for straightforward platform-switched implant placement.

2- There are no differences in pain severity, surgery-associated morbidities, and one-year implant survival rate between healthy patients who received a pre- and postoperative antibiotic regimen compared to those who received only a preoperative dose of antibiotics during surgery for straightforward platform-switched implant placement.

2.2 RESEARCH METHODOLOGY

2.2.1 Study design, participants, eligibility and intervention

The study used double-masked two-arm randomized controlled clinical trial.

Fifty patients from the Dental Clinic at the Faculty of Dentistry of the Université de Montréal were invited to participate in this study. The eligibility criteria are presented in Table 2.

Table 2: Inclusion and exclusion criteria

Inclusion criteria:
- Periodontally healthy remaining dentition or presenting with mild gingivitis with adequate oral hygiene. - Presence of a partially edentulous alveolar ridge that will be restored with no more than two adjacent implants. - To have one or two implants restored with a crown or fixed bridge. - Absence of any active infection in site. - Presence of enough bone and soft tissue for the implant to be placed without any bone grafting procedure in a one-stage approach (with healing abutment). - Implants 8 mm long or longer using the Dentsply AstraTech Implant System™ (Osseospeed TX or EV™). - Subjects able and willing to provide written informed consent and comply with study procedures.
Exclusion criteria:
- Individuals taking regular analgesics or antidepressants. - Allergies to amoxicillin, cephalosporin, 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 uncontrolled 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 three 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.

Eligible participants were randomized in two groups using block randomization. Individuals in the intervention group received 2 g of amoxicillin one hour prior to surgery and 500 mg three times a day for seven days. Those in the control group received only 2 g of amoxicillin one hour prior to surgery and an identical placebo three times a day for seven days.

Prior to data collection, the ethics committee for health research at the Université de Montréal (Comité d'éthique de la recherché en santé: 13-094-CERES-D) approved this study, which was registered at www.clinicaltrials.gov (NCT01851681). All study procedures were undertaken with the understanding and written consent of each participant and in accordance with ethical principles including the World Medical Association Declaration of Helsinki (Appendix I). The participants were informed of the sequence, duration and number of appointments they would need to attend in order to remain in the study (Appendix II).

2.2.2 Outcomes measures

The primary outcome was the changes in crestal bone level measured by periapical radiographs using a standardized technique at baseline and at four-month follow-up. The secondary outcomes were pain severity, surgery-associated morbidities (interference with

daily activities, swelling, suppuration, ecchymosis, dehiscence, infection, neuropathy, paresthesia, mobility and radiolucency) evaluated by clinical examination and self-administered questionnaires, and one-year implant survival rate. The explanatory variables included the participants' sociodemographics and medical background such as mean age, sex, language, ethnic background, civil status, living status, education, yearly household income, smoking status, and diabetes. They also included surgical parameters such as the number of implants per patient, mean surgery duration, mean incision length, mean bone quality, implant location, as well as implant characteristics such as implant diameter, implant length, insertion torque and implant system.

2.3 DATA COLLECTION AND EXPERIMENTAL PROCEDURES

2.3.1 Medical and sociodemographic questionnaires

A research assistant approached and recruited patients who were willing to restore a partially edentulous area with a fixed implant prosthesis at the implantology clinic of the Faculty of Dentistry at the Université de Montréal. Medical history, smoking habits, and sociodemographic data were obtained through self-administered questionnaires (Appendices III and IV).

2.3.2 Clinical procedures

All participants were instructed to rinse with chlorhexidine gluconate 0.12% for one minute, and were given 600 mg of ibuprofen and 2 g of amoxicillin one hour prior to surgery under the supervision of a research assistant. 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, Osseospeed™ TX Profile or Astra EV™, Dentsply Implants, Mölndal, Sweden) were placed in a one stage procedure without simultaneous bone grafting, in accordance with the manufacturer's recommendations, by two board-certified specialists who had a minimum of 10 years of experience in surgical implantology. Mucoperiosteal flaps were raised to access the underlying alveolar bone for all implant surgeries. The healing abutment was inserted at the time of implant placement and soft tissues were sutured with interrupted sutures (4-0 silk, Perma Sharp®, Hu-Friedy Mfg Co., Chicago, IL, U.S.A.). A standardized radiograph was taken immediately after dental implant placement. The research assistant placed the x-ray cone perpendicular to the crestal bone to assess the baseline crestal bone level on the mesial and distal aspects of each implant using a bite registration material (Blu-Mousse®, Parkell Inc., Edgewood, NY, U.S.A.) adapted to a paralleling device (XCP film holding system, Dentsply Rinn, Elgin, IL, U.S.A.) for each participant (Figure 1). The customized bite registrations with each participant's study identification number were kept in a locked cabinet in a cool room for the subsequent four-month follow-up period. Surgical parameters such as the length of the incision, implant system, implant dimensions, insertion torque, bone quality (83), and the duration of the surgery were recorded by the surgeon. Participants were asked to refrain from performing mechanical plaque control in the surgical area and were advised to remain on a soft diet during the first postoperative week.

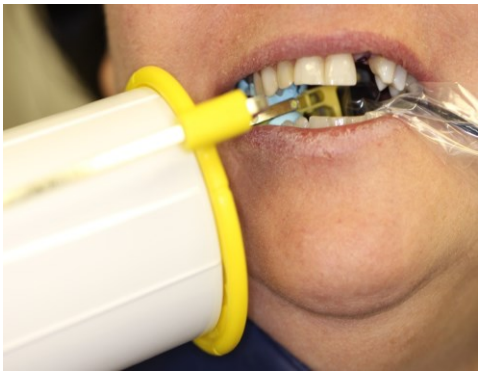

Figure 1: Individualized silicon bite block and x-ray positioning technique

Randomized subject allocation was done in blocks of six subjects by a computer-generated sequence and sealed in consecutively numbered opaque envelopes by a research assistant who was the only person aware of each subject's group allocation. To standardize postoperative procedures, all participants were prescribed 600 mg of ibuprofen to be taken every four hours for the first 48 hours with a maximum of four tablets per day. They were also prescribed an emergency analgesic (500 mg acetaminophen) to take 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. Prior to dismissal, each participant received written postoperative instructions (Appendix V) along with an envelope bearing the participant's study number that contained the antibiotic and analgesics to be taken postoperatively as well as specific instructions on how to take their medication, so the investigators were unaware of the antibiotic regimen. After receiving standardized verbal and written postoperative instructions, participants were given questionnaires to assess their perceived pain experience and interference with several daily activities as well as an analgesic intake diary to be filled out during the first postoperative week. The patient's pain experience was also assessed with a 10-cm VAS questionnaire (0-10), with "0" representing "no pain"

and “10” representing “the most intense pain imaginable”, along with the daily pain medication intake diary. Participants were asked to record their experience regarding the interference with their daily activities using a 10-cm VAS questionnaire, with a score of “0” representing “no interference” and a score of “10” representing “extremely much” (79). Daily activities included the ability to chew foods they wanted to eat, to open their mouth wide, talk, sleep, go to school or work, carry on a regular social life and participate in their favourite recreational activities. The participants were asked to bring back to the research assistant at the one-week follow-up (T1) the pain and daily interference questionnaires as well as the pain medication diary, the envelope and the drug containers to ensure their compliance with the prescriptions. At the postoperative control appointment, an examiner who was unaware of the antibiotic regimen prescribed filled a form to evaluate swelling, bruising, pus exudates and wound dehiscence as described elsewhere (79). Postoperative swelling was graded as follows: 0 = No swelling, 1 = Mild swelling, 2 = Moderate swelling, 3 = Severe swelling. Postoperative bruising, suppuration and wound dehiscence were evaluated using Boolean variables: 0 = None; 1 = Present. The examiner measured the modified plaque index (mPI) (84) at four sites per implant (mesial, distal, buccal, lingual). The mPI was graded as follows: 0 = no detection of plaque, 1 = Plaque only detected by running a probe (PCP-UNC15; Hu-Friedy Mfg Co., Chicago, IL, U.S.A.) along the smooth surface of the healing abutment, 2 = Plaque can be seen by the naked eye, 3 = Abundance of soft matter. The mPI was also measured at the three-week and sixteen-week examinations. At the three-week follow-up (T2), postoperative swelling, bruising, suppuration and wound dehiscence were evaluated as well as the mPI. At the sixteen-week evaluation (T3), the implants were evaluated clinically using the Albrektsson implant success criteria (25) along with the mPI, and radiographically to confirm the absence of

radiolucent lesions and assess the peri-implant crestal bone level. This appointment usually coincided with the impression for the implant restoration. The masked examiner took a standardized periapical radiograph using the individualized bite registration and the paralleling device. He assessed implant mobility using the handles of two blunt dental instruments (27) (osseointegration = immobile, failure = mobile) and evaluated the presence or absence of any symptoms related to infection (suppuration), inflammation (erythema, bleeding on probing) or neuropathy (paresthesia, dysesthesia, anesthesia). At least eight months after the implant was restored, the same examiner assessed implant mobility, peri-implant health by probing depth at four sites per implant, and the presence or absence of any symptoms related to infection in order to evaluate the one-year success rate for each group.

2.3.3 Radiographical methodology

The radiographic images were sent to the Medical Research Center of the Université de Montréal (CRCHUM) in order to be repositioned so that the baseline image could be superimposed to the four-month image. In order for all images to be standardized and subsequently superimposed, they had to be digitally manipulated in a Matlab® environment (Mathworks®, Natick, MA, U.S.A.) by an expert who was unaware of group allocation. More specifically, an intensity-based registration method was used. It compared the pixel values by using an image similarity measure based on image statistics. This measure quantifies the degree of similarity between the intensity patterns of two images. The similarity metric selected for the registration was mutual information. This method is designed to match data points by finding the mutual dependence between the source image and the target image.

Mutual information *S* is given by:

$$S = \sum_{x,y} p(x,y) \log \frac{p(x,y)}{p(x)p(y)}$$

where *p(x)* and *p(y)* are the probability distributions in individual images and *p(x,y)* is the joint probability distribution. Mutual information does not assume a linear relationship between the pixel values of the two images, but instead assumes that the co-occurrence of the most probable values in the two images is maximized at registration. Optimal mapping could be obtained by a simple rotation and translation.

Once the standardized images were processed, an examiner unaware of the intervention allocation drew a long axis on each implant and a perpendicular horizontal line from that axis to the first bone-to-implant contact point on the mesial and distal areas of each implant. Once these horizontal lines were drawn, the images were superimposed and the difference in distance between the baseline and the four-month postoperative images was measured using an image processing software at high magnification (~ 3400%) (Adobe Illustrator CC 2017, Adobe Systems Inc., San Jose, CA. U.S.A.).

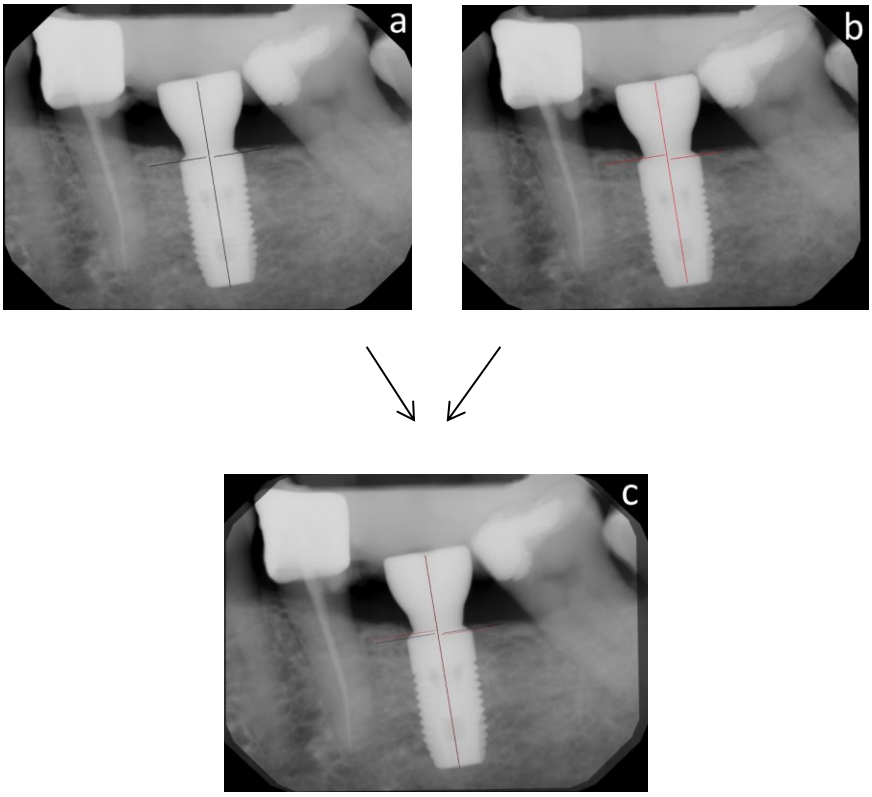

Figure 2: Radiographic evaluation of crestal bone change: a) Baseline periapical radiograph; b) four-month periapical radiograph; c) Superimposed radiographs with baseline and four-month measurements.

2.4 STATISTICAL ANALYSIS

The intra-examiner agreement for the radiographical assessment of the crestal bone level change was evaluated by using an intraclass correlation coefficient (ICC) with a value > 0.90 representing excellent agreement. 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. An average value was used when a patient received two implants for crestal bone level change, plaque index and surgical parameters. The implant with the worst outcome was used for swelling, ecchymosis, suppuration and dehiscence. A Pearson correlation was used to assess the relationship between surgery duration and crestal bone level changes. SPSS version 24 was used for analyses. A p value ≤ 0.05 was considered statistically significant.

Assuming that the difference in crestal bone level change between the study groups would be 0.5 mm with a standard deviation of 0.5 mm, the sample size of 17 participants in each group would provide a power of 80% to reject the null hypothesis of absence of the differences between group if it is indeed false, at an alpha level of 5%. This difference of 0.5 mm is generally considered to be clinically significant (40).

2.5 ETHICAL CONSIDERATIONS

To make sure patients at the implantology clinic did not feel obligated to participate in this study, a research assistant gave potential participants written information about the ongoing study at our clinic (Appendix VIII). The implantology coordinator reminded the patients who had decided to take part in the study prior to surgery since there was often a significant delay

between the recruitment and the implant surgery appointment. On the day of the surgery, participants read and signed the informed consent form while they were in the waiting room and a research assistant was available to answer their questions.

Since the dental record number of each participant was written on the questionnaires for identification purposes, a research assistant removed the dental record number and replaced it with a study code prior to data analysis. She then placed the questionnaires in a folder containing only the study number of each participant. The folders containing the research data were kept in a locked office at the Université de Montréal. During the entire process of data collection, the principal investigator ensured that the research team followed the rules of ethics and that only members of the research team had access to the room where the data was kept. The research assistant was the only person who had the sheet where dental record numbers were matched with study codes**.**

2.6 STUDY RELEVANCE

To our knowledge, this is the first placebo-controlled clinical trial evaluating the influence of postoperative antibiotics on peri-implant crestal bone remodeling. The evidence will provide clinical guidelines with regards to the perioperative antibiotic regimen for implant placement. This may change current practices in implant dentistry and protect patients from the effects of antibiotics overuse. Moreover, this phase-I clinical trial will help the conceptualization of future research in this area.

CHAPTER III

RESULTS

3.1 RECRUITMENT OF PARTICIPANTS

Figure 3 shows the study flowchart. Fifty patients were initially asked to participate in the study. Thirty-eight patients were eligible to take part in the study and were randomly selected to be either in the intervention or the placebo group. One study participant was excluded from the statistical analysis because of non-compliance.

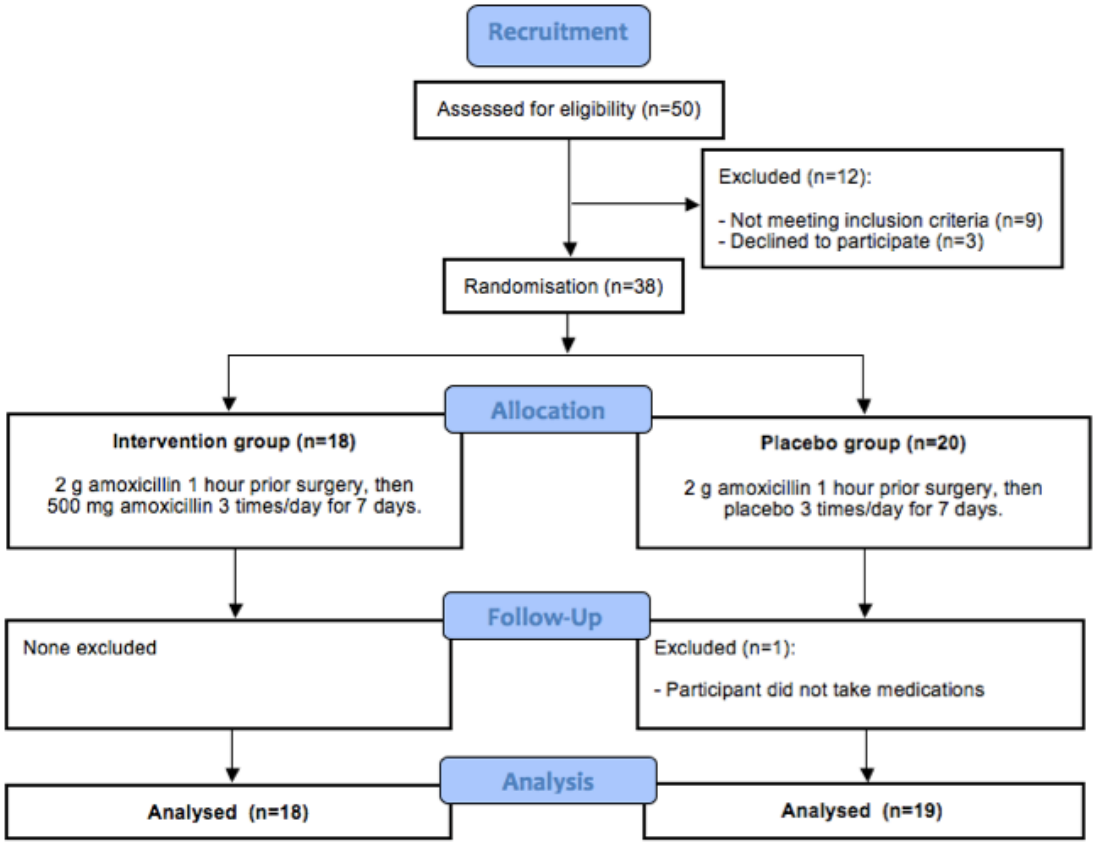

Figure 3: Study flowchart

3.2 CALIBRATION RESULTS

The intra-examiner calibration reliability for radiographic measurements of crestal bone changes was excellent. The intraclass coefficients were 0.998 and 0.997 for the mesial and distal aspect of implants, respectively.

3.3 SOCIODEMOGRAPHICS AND MEDICAL BACKGROUND

Table 3 shows the participants' sociodemographics and medical background by intervention group. The mean age of participants was 57.4 ± 11.3 years. There were no statistically important differences between the groups concerning any of the sociodemographic variables. Most participants were French-speaking, of North American or European descent and were born in Canada. There were also no significant differences between the groups regarding the smoking and diabetes status. Only one participant in the placebo group was a smoker.

Table 3: Participants' sociodemographics and medical characteristics

Variables	Intervention (n=18)	Control (n=19)	P value
Mean age: (years, ±SD)	55.5±9.1	59.1±13.1	0.347
Sex (n, %):			
- Female	11 (61.1)	10(52.6)	0.743
- Male	7 (38.9)	9 (47.4)	
Language: (n,%):			
- French	15(83.3)	13 (68.4)	0.566
- English	0 (0.0)	1 (5.3)	
- Other	3 (16.7)	5 (26.3)	
Ethnic background (n,%):			
-North America	10(55.6)	9 (47.4)	0.721
-Europe	7 (38.9)	7 (36.8)	
-Other	1 (5.6)	3 (15.8)	
Civil status (n,%):			
- Married	13 (72.2)	10 (52.6)	0.313
- Other	5 (27.8)	9 (47.4)	
Living status (n,%):			
-Alone	2 (11.1)	4 (21.1)	0.635
-Live with family	15 (83.3)	13 (68.4)	
-Other	1 (5.6)	2 (10.5)	
Education (n, %):			
- University	10 (55.6)	12(63.2)	0.743
- College or less	8 (44.4)	7 (36.8)	
Yearly household income (n, %):			
- ≥ $50,000	10 (55.6)	12 (63.2)	1.000
- < $50,000	6 (33.3)	6 (31.6)	
-Did not answer	2 (11.1)	1 (5.3)	
Currently smoking (n, %):			
-Yes	0 (0.0)	1 (5.3)	1.000
-No	18 (100)	18 (94.7)	
Former smoker (n, %):			
-Yes	8 (44.4)	9 (47.4)	1.000
-No	10 (55.6)	10 (52.6)	
Diabetes (n, %):			
-Yes	1 (5.6)	2 (10.5)	1.000
-No	17 (94.4)	17 (89.5)	

3.4 SURGICAL PARAMETERS AND IMPLANT CHARACTERISTICS

Table 4 represents the subject-based analysis of surgical parameters and implant characteristics between the intervention and control groups. There was a significantly higher number of participants receiving two implants in the placebo group compared to the intervention group (P = 0.038). Implant surgeries also lasted on average significantly longer in the placebo group (P = 0.021). There were no significant differences between the groups concerning the other surgical parameters and any of the implant characteristics.

Table 4: Surgical parameters and implant characteristics

Variables	Intervention (n=18)	Control (n=19)	P value
Patients having (n, %): -One implant -Two implants	 15 (83.3) 3 (16.7)	 9 (47.4) 10 (52.6)	**0.038**
Mean implant diameter (mm, ±SD)	4.65±0.64	4.48±0.62	0.388
Mean implant length (mm, ±SD)	10.28±1.53	10.47±1.17	0.869
Mean insertion torque (Ncm, ±SD)	39.72±8.99	41.32±6.15	0.503
Mean surgery duration (min, ±SD)	43.5±13.2	57.6±21.1	**0.021**
Mean incision length (mm, ±SD)	20.0±6.6	22.5±6.7	0.267
Mean bone quality (category, ±SD)	2.6±0.5	2.42±0.8	0.455
Implant location (n, %): - Maxilla - Mandible	 9 (50.0) 9 (50.0)	 9 (47.4) 10 (52.6)	1.000
Implant system (n, %): - Astra Tech TX™ - Astra Tech EV™	 9 (50.0) 9 (50.0)	 9 (47.4) 10 (52.6)	1.000

3.5 PERI-IMPLANT CRESTAL BONE CHANGE

Figures 4 and 5 show the mean radiographic crestal bone changes between groups. There was a significant additional loss of 0.30 mm for the mean mesial crestal bone loss in the intervention group compared to the placebo group (P = 0.014) but no significant differences regarding the mean distal crestal bone change. In the intervention group, the mean combined crestal bone change was -0.29±0.36mm while it was -0.11±0.35mm for the placebo group, and this difference was not significant (P = 0.134).

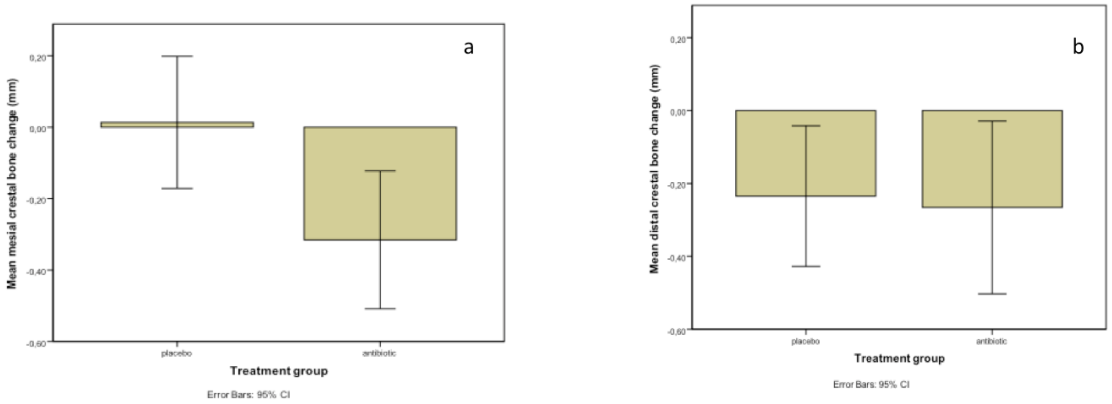

Figure 4: Mean crestal bone changes after four months: a) At the mesial aspect; b) At the distal aspect.

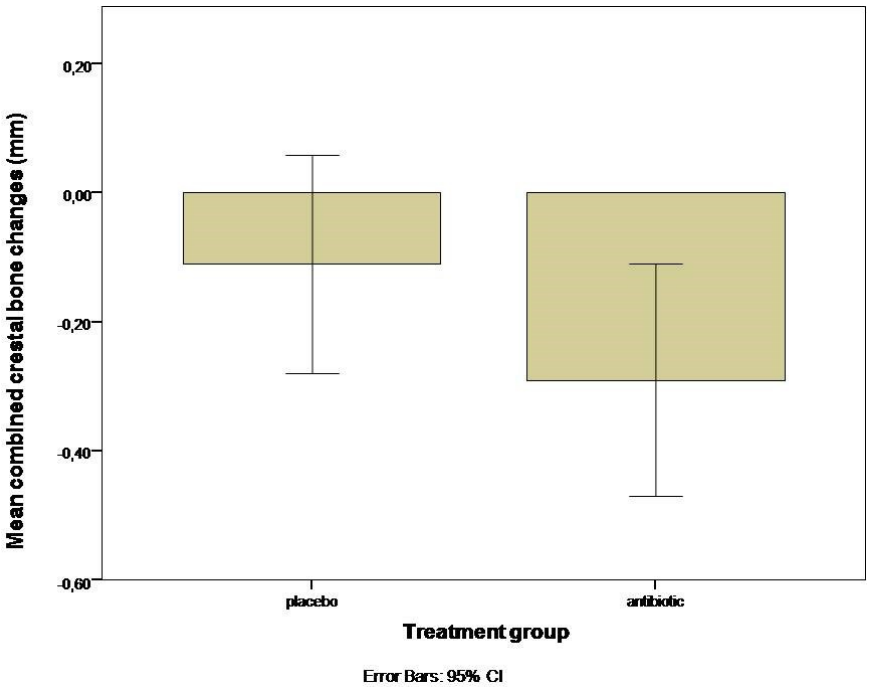

Figure 5: Mean combined crestal bone changes after four months

3.6 PAIN EXPERIENCE

Figures 6 and 7 show the participants' perceived pain during the first twelve hours and seven days after surgery. The perceived pain intensity was overall mild (VAS score = 1-3) in both groups. The median pain intensity for both the placebo group and the intervention group reached a peak 24 hours after surgery (Figure 6). There was no perceived pain after the morning of the third day in the intervention group and the level remained the same for the rest of the postoperative healing period (Figure 7). In the placebo group, the perceived pain reached the "zero" value after the morning of the sixth day. On several occasions during the first seven postoperative days, the median pain score was 2 in the placebo group while it was 0 in the intervention group. More specifically, this difference was statistically significant on the fourth day at noon ($P = 0.047$) and at night ($P = 0.036$), and on the fifth day at night ($P = 0.036$). The mean number of emergency analgesics given to 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 groups ($P = 0.864$).

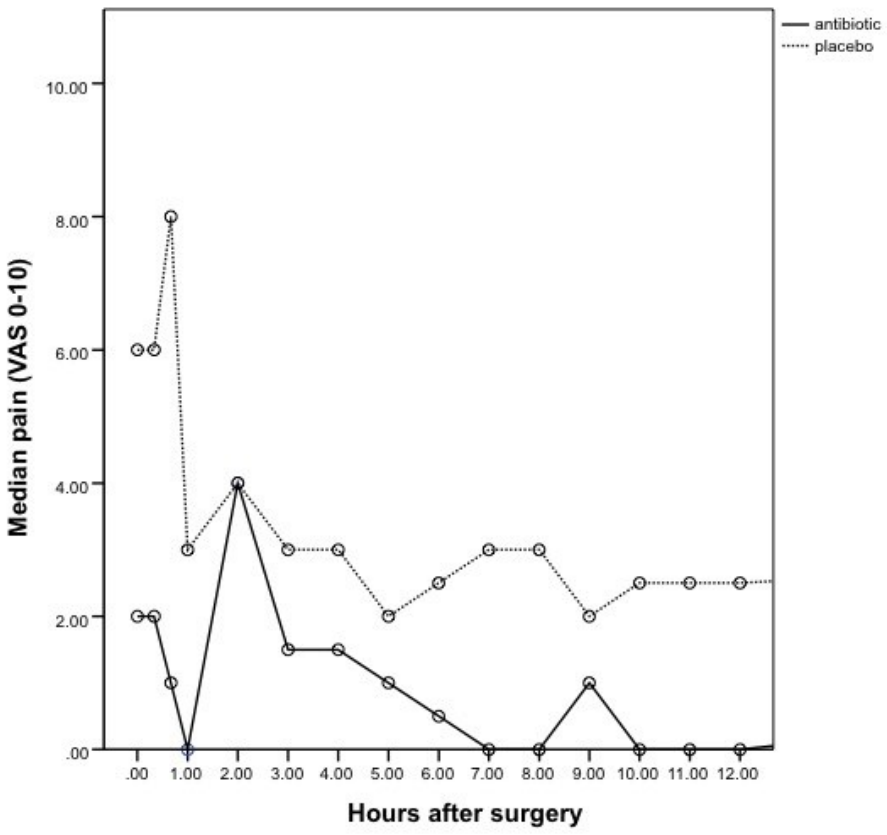

Figure 6: Pain severity for the first twelve hours after surgery

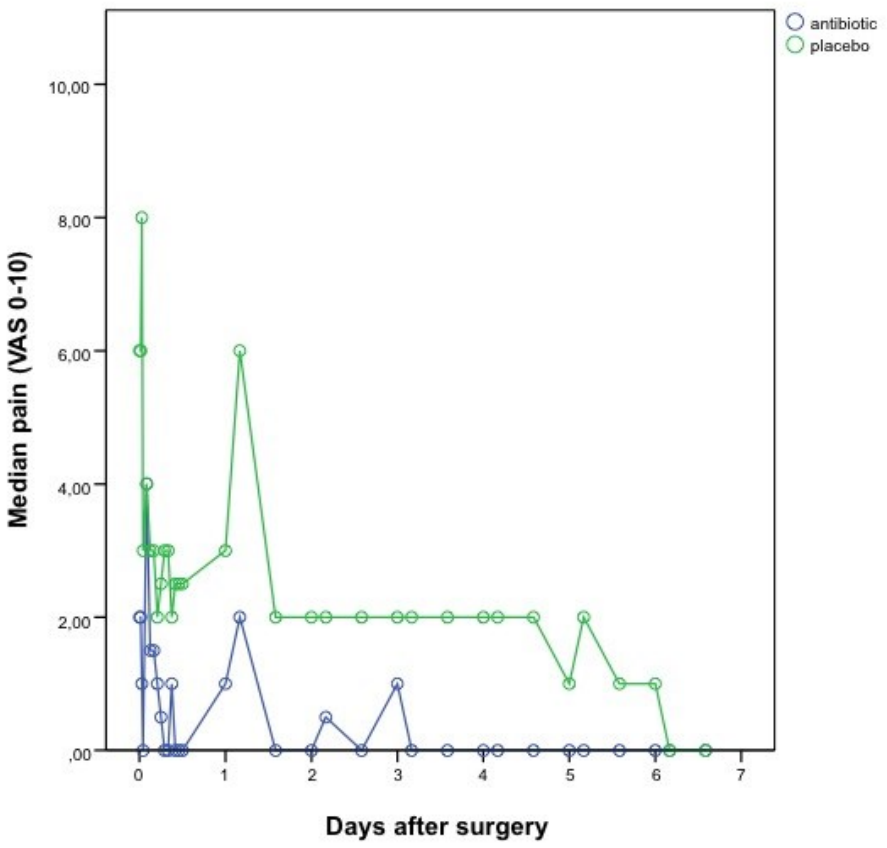

Figure 7: Pain severity for the first seven days after surgery

3.7 INTERFERENCE WITH DAILY ACTIVITIES

Figures 8 to 14 represent the patients' subjective experience concerning the surgery's interference with daily activities during the first seven days after implant placement. There was significantly more interference with chewing in the placebo group on the seventh postoperative day (Figure 8). The participants taking a placebo after surgery had much more difficulty opening their mouth as of the third postoperative day onward (Figure 9). No statistically significant differences were found between the groups regarding speech during the first seven days after surgery (Figure 10). From the third to the sixth day after surgery, participants in the placebo group experienced significantly more interference with sleep compared to the participants who had taken an antibiotic postoperatively (Figure 11). The same findings were seen on the fifth, sixth and seventh days after surgery regarding the interference with work or school, and social activities (Figures 12 and 13). Participants in the placebo group experienced significantly more interference with recreational activities than those in the antibiotic group during the fifth and sixth days after surgery (Figure 14).

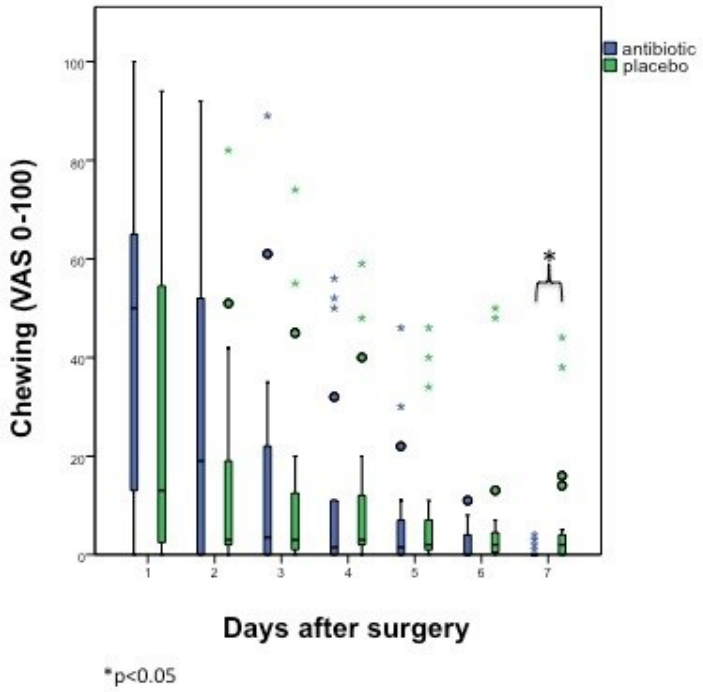

Figure 8: Interference with chewing

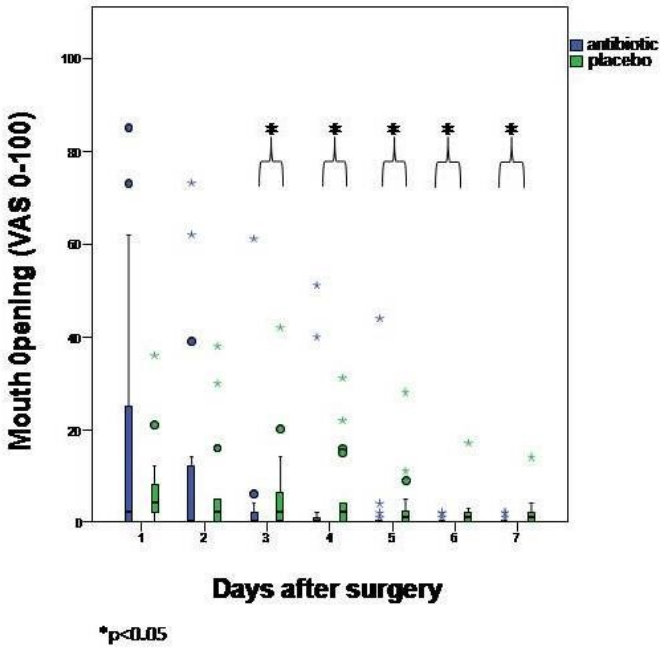

Figure 9: **Interference with mouth opening**

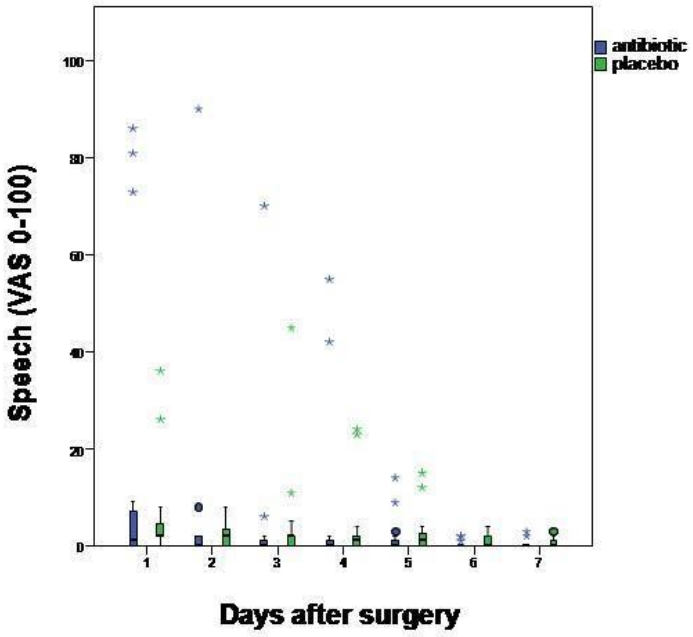

Figure 10: Interference with speech

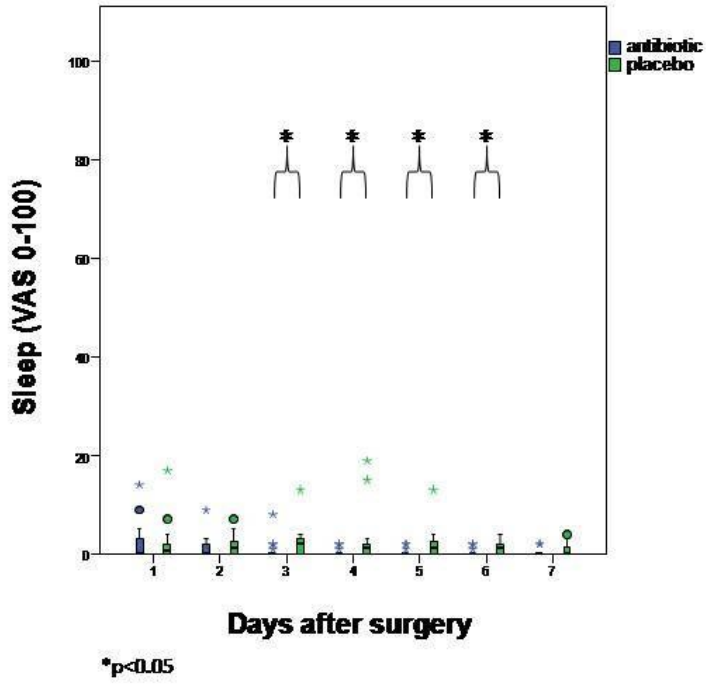

Figure 11: Interference with sleep

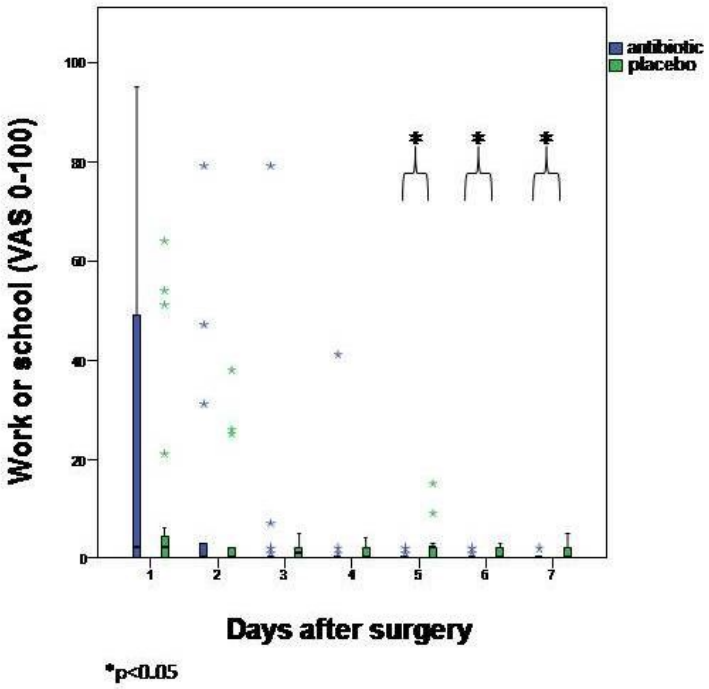

Figure 12: Interference with work or school

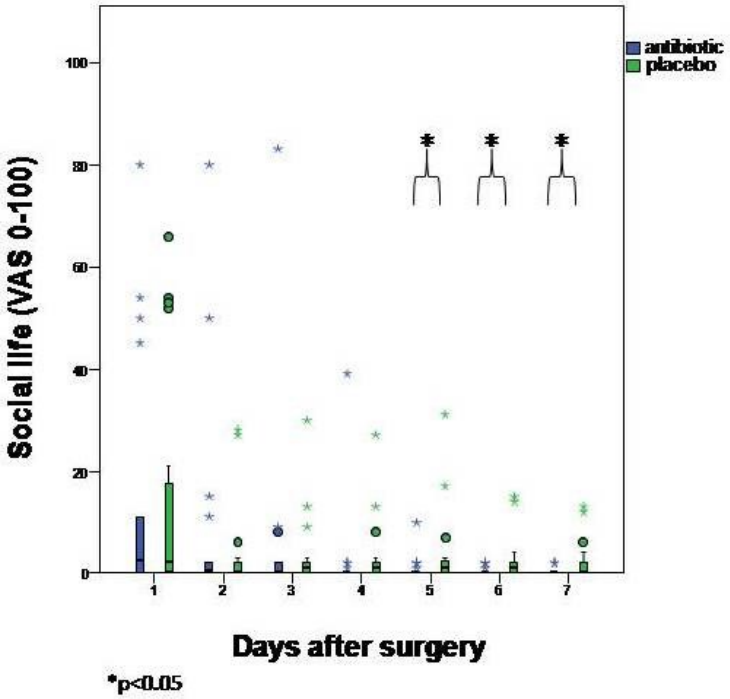

Figure 13: Interference with social life

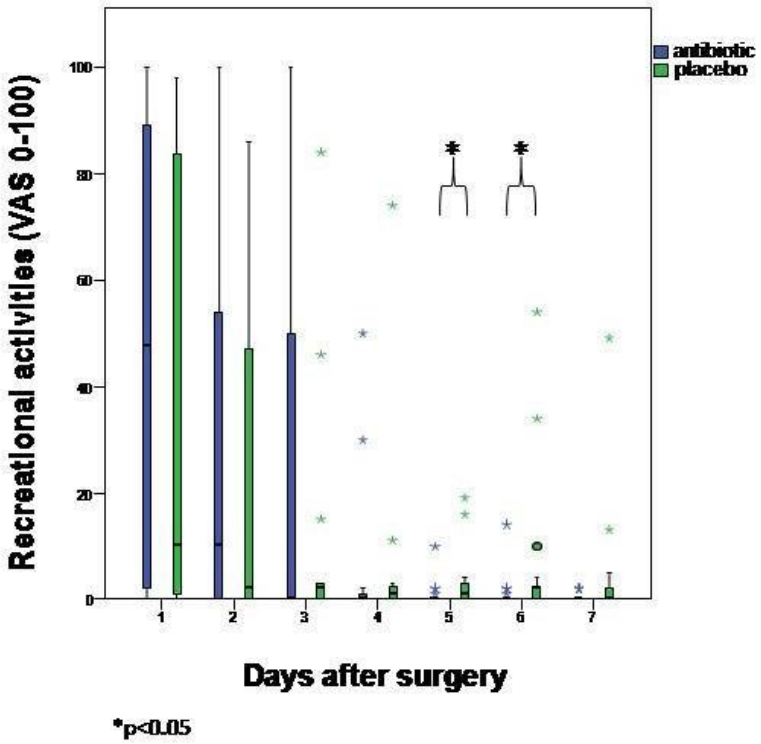

Figure 14: Interference with recreational activities

3.8 POSTOPERATIVE MORBIDITIES

Tables 5, 6 and 7 show postoperative morbidities on the one-, three-, and sixteen-week follow-up exams. There were no statistically significant differences between the groups regarding any of the parameters measured. Two patients in the intervention group developed suppuration at the one-week examination and were advised to rinse with a 0.12% chlorhexidine solution bid x two weeks (Table 5), which controlled their condition and they did not develop further complications. On the sixteen-week follow-up, one patient in the intervention group had developed a gingival abscess with suppuration that was caused by food impaction on the area. Subgingival curettage under local anesthesia was immediately undertaken and the patient was prescribed a chlorhexidine rinse to use for four weeks. The patient was reevaluated four weeks later and the abscess had subsided. More importantly, the implant survival rate was 100% on the one-year follow-up examination in both groups, with all implants in function for at least six months and peri-implant probing depth ≤ 5 mm in all sites, and patients exhibiting healthy peri-implant tissues. Only one side effect was reported: one participant in the placebo group reported diarrhea two days after surgery. This complication was most likely associated with the 48-hour 600 mg ibuprofen regimen that was given to all participants for postoperative analgesia.

Table 5: Postoperative morbidities after one week

Variable	Intervention (n=18)	Control (n=19)	P value
Swelling (n,%): No Yes	 18 (100.0) 0 (0.0)	 17 (89.5) 2 (10.5)	0.486
Ecchymosis (n,%): No Yes	 18(100.0) 0 (0.0)	 17 (100.0) 0 (0.0)	1
Suppuration (n,%): 0 1	 16 (88.9) 2 (11.1)	 17 (100.0) 0 (0.0)	0.230
Dehiscence (n,%): 0 1	 15 (83.3) 3 (16.7)	 19 (100.0) 0 (0.0)	0.105

Table 6: Postoperative morbidities after three weeks

Variable	Intervention (n=18)	Control (n=19)	P value
Swelling (n,%): - No - Yes	 18 (100.0) 0 (0.0)	 19 (100.0) 0 (0.0)	1
Ecchymosis (n,%): - No - Yes	 18 (100.0) 0 (0.0)	 19 (100.0) 0 (0.0)	1
Suppuration (n,%): - No - Yes	 18 (100.0) 0 (0.0)	 19 (100.0) 0 (0.0)	1
Dehiscence (n,%): - No - Yes	 18 (100.0) 0 (0.0)	 19 (100.0) 0 (0.0)	1

Table 7: Postoperative morbidities after 16 weeks

Variable	Intervention (n=18)	Control (n=19)	P value
Infection (n,%):			
- No	17 (94.4)	19 (100.0)	
- Yes	1 (5.6)	0 (0.0)	0.486
Suppuration (n,%):			
- No	17 (94.4)	19 (100.0)	
- Yes	1 (5.6)	0 (0.0)	0.429
Pain (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0 (0.0)	0 (0.0)	1
Neuropathy (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0 (0.0)	0 (0.0)	1
Paresthesia (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0 (0.0)	0 (0.0)	1
Mobility (n,%):			
- No	18 (100.0)	19 (100.0)	1
- Yes	0 (0.0)	0 (0.0)	
Radiolucency (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0 (0.0)	0 (0.0)	1

Table 8: Postoperative morbidities after one year

Variable	Intervention (n=18)	Control (n=19)	P value
Infection (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0(0.0)	0 (0.0)	1
Suppuration (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0(0.0)	0 (0.0)	1
Pain (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0 (0.0)	0 (0.0)	1
Neuropathy (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0 (0.0)	0 (0.0)	1
Paresthesia (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0 (0.0)	0 (0.0)	1
Mobility (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0 (0.0)	0 (0.0)	1
Radio lesion (n,%):			
- No	18 (100.0)	19 (100.0)	
- Yes	0 (0.0)	0 (0.0)	1

3.9 ORAL HYGIENE AROUND IMPLANTS

Table 9 shows that most participants maintained good oral hygiene around the implants throughout the study, with a mean mPI below 1.0 for both groups at all time points. No significant differences were seen between the groups, except at the three-week follow-up examination when participants in the placebo group had significantly more plaque than those in the intervention group (P=0.035).

Table 9: Modified plaque index (mPI)

mPI	Intervention (n=18)	Control (n=19)	P value
After one week (±SD)	0.4±0.3	0.4±0.4	0.861
After three weeks (±SD)	0.3±0.7	0.4±0.3	0.035
After 16 weeks (±SD)	0.2±0.2	0.2±0.3	0.692

3.10 EFFECTS OF SURGERY DURATION AND NUMBER OF IMPLANTS ON CRESTAL BONE CHANGE

Surgeries lasted significantly longer in the placebo group than in the intervention group, and the number of participants receiving two implants was significantly higher. Therefore, a two-sample t-test was done and it was found that the number of implants placed during surgery significantly increased the surgery duration (two implants (n=13): 66.6±17.0 min. *vs* one implant (n=24) : 42.1±13.7 min., P<0.001). Subsequently, a regression model was used to investigate the effects of surgery duration on crestal bone level changes (Figure 15). It was found that surgery duration had no significant effect on the crestal bone level change (Pearson's correlation R=0.028, R^2=0.0008, P=0.871).

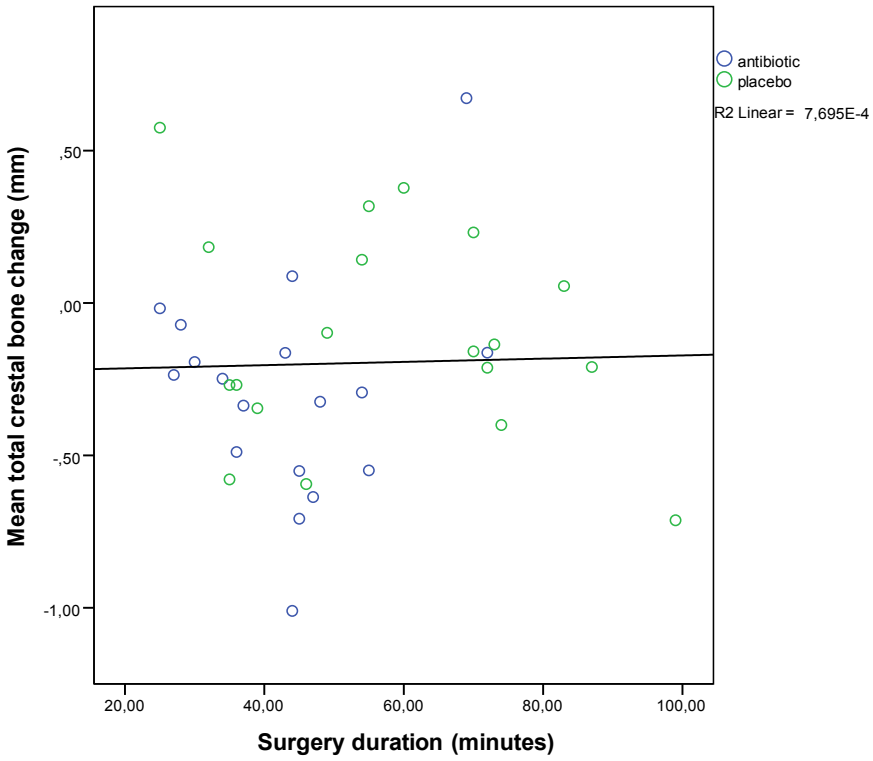

Figure 15: Correlation between surgery duration and crestal bone level change

CHAPTER IV

DISCUSSION

To our knowledge, this is the first double-masked randomized clinical trial aimed at evaluating the effects of postoperative antibiotics on peri-implant bone remodeling. The results of this study showed that adding a postoperative regimen of amoxicillin for seven days provided no apparent benefit during a four-month peri-implant bone remodeling, nor for the perceived pain experience, postoperative morbidities and one-year implant survival rate in healthy patients undergoing straightforward platform-switched implant placement.

4.1 CLINICAL OUTCOMES

This study found no significant difference in mean combined crestal bone level change between the intervention and the control groups. The Dental Implant Clinical Research Group study that included 1,762 implants placed in individuals from 32 Department of Veterans Affairs medical centers and university research clinics support these results (12). The authors found 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 available. Consequently, they speculated that these findings were probably due to the fact that the decision to give postoperative antibiotics was left to the surgeon. This decision was most likely influenced by the surgery's complexity and the patient's systemic condition, which could be associated with further peri-implant bone loss rather than the postoperative antibiotic regimen itself. However, our worst scenario, i.e. a longer surgery with higher number of

implants (2 *vs* 1), showed that the peri-implant bone loss was not associated with the surgery's complexity.

In vitro studies have also showed that several commonly given antibiotics have a negative effect on bone remodeling by reducing the number of human osteoblasts by more than 50% (85). More specifically, with minocycline, doxycycline, penicillin and ciprofloxacin at concentrations ≤ 200 µg/ml, osteoblasts counts, alkaline phosphastase (ALP) levels, and osteogenic activity markers were reduced. However, benzyl-penicillin (same family as amoxicillin) has not shown to have any effect on mesenchymal cell proliferation and differentiation towards an osteogenic lineage (86). These results are in line with the findings of our study. While most *in vitro* and animal studies reporting impairment of osteoblastic cell functions involved higher antibiotic doses than those used in oral administration, it should be mentioned that higher plasma concentrations can be reached with consecutive systemic doses and that a single dose was used in most of the published studies (87).

In our study, the differences between groups were only significant for peri-implant bone loss at the mesial region of implants. This result can be explained by the difference of subcrestal positions in a crestal slope where more peri-implant bone loss might be observed, a situation found mainly in the posterior maxilla and mandible. However, a recent clinical study demonstrated that titled implants did not exhibit more peri-implant crestal bone loss than non-tilted implants (88). Therefore, this explanation is still debatable because the standardization of surgical procedures as well as the results of clinical studies where implants were tilted do not lead to further peri-implant bone loss.

The absence of a statistically significant difference of mean combined crestal bone change between groups may be explained by several factors. First, platform-switched implants have shown minimal bone remodeling compared to implants with regular platforms (89). A recent systematic review has shown that the mean peri-implant crestal bone loss around implants with internal connections varied from 0.07 to 0.87 mm (90) and our findings are well within that range. Furthermore, the surgeons involved in this study all had a minimum of 10 years of experience and performed the implant surgeries under standardized conditions. This helped minimize performance bias. In fact, a surgeon's years of experience and skill level are associated with a decrease in early implant failure rate (91). However, our results should be interpreted with caution since our population was healthy and the implant surgeries were not complex and did not involve additional bone grafting procedures. Therefore, results should not be generalized to include patients who are smokers, bruxers, medically compromised, as well as more complex surgeries.

The results from this study showed that there were no significant differences in postoperative morbidities and implant survival rates between the groups. Other studies comparing pre- *vs* pre- and post-operative intake of antibiotics for the prevention of implant complications have demonstrated similar results (7, 80-82). In the Tan et al. multicenter investigation, only those patients who had not taken any perioperative antibiotics did not achieve complete wound closure at the fourth postoperative week (81). The authors questioned the necessity of giving antibiotics before, at the time of or after implant placement to improve the implant survival rate, at least in straightforward implant surgeries, which characterized their patient population as well as ours. A recent systematic review has concluded that although the use of antibiotic

prophylaxis reduced the risk of implant loss by 2%, it did not provide any benefit for uncomplicated implant surgery in healthy patients while a beneficial effect in uncomplicated cases could not be excluded (11). However, one might want to keep in mind that it is not always possible to determine ahead of time if the implant surgery will indeed be an uncomplicated one, even if the patient is healthy. Moreover, several etiological factors unrelated to the patient's health or the surgery's complexity have been reported to play a role in increasing the 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 (92, 93).

4.2 PATIENT-BASED OUTCOMES

In this study, the control group experienced significantly higher pain severity compared to the intervention group on the fourth and fifth days after surgery. This difference could be explained by the fact that the implant surgeries lasted significantly longer for the participants taking the placebo than for those who took the postoperative antibiotic regimen since there were significantly more participants receiving two implants in the control group. Indeed, it was shown that postoperative pain was significantly correlated with implant surgery duration (67, 94). Another important factor was that the number of implants was higher in the control group. Patients having a greater extension of the surgical site were found to be more susceptible to experiencing severe pain (VAS score = 7-10) (94). This was illustrated by the participants taking the placebo and having a VAS median pain of 8 one hour after surgery. Nevertheless, the overall median pain severity observed during the first seven days after

surgery in both groups was considered mild (VAS score = 1-3). This finding was similar to those of other studies done under similar conditions where most of the time an experienced surgeon placed a single implant without any associated complex surgery (62, 66, 81). Also, the median implant surgery duration in both groups was less than an hour, which could explain the low postoperative pain severity.

The control group also experienced significantly more interference with daily activities seven days after surgery compared to the intervention group. One might expect this difference since the experienced pain severity was higher among these participants. Pain is a major life-affecting factor that will inevitably influence an individual's quality of life. More specifically, interference with sleep was significantly higher in the control group from the third to the sixth postoperative day. On the seventh day, the difference was no longer significant and this decline was consistent with the decrease in the pain experienced, which was also no longer significantly different between the groups. Nolan et al. reported that patients experiencing higher pain and interference with daily activities after two and seven days were more susceptible to experience implant failure (79). Importantly, all five failures in their study occurred in participants who did not take any antibiotic prior to implant placement. Our study did not demonstrate such an association most likely because of the small sample size, probably because only experienced surgeons placed the implants, and potentially because all participants took a preoperative dose of antibiotics.

4.3 STUDY STRENGTH AND LIMITATIONS

This study is a pilot study toward a phase-II randomized clinical trial. Phase-I trials are conducted to evaluate an intervention in a small group of participants in order to standardize study procedures, assess the safety of the intervention, assess the recruitment process, collect preliminary data for future sample size calculations, assess the practicality of a multicenter study, and guide the development of a future trial with a larger sample size (95-97). This pilot study allowed us to standardize our study procedures for a larger phase-II trial.

Although randomized block allocation was used to divide participants among the study groups, the worst-case strategy used in this pilot trial gave us the opportunity to test our hypotheses under surgical conditions that may lead to worse outcomes. Our study sub-analysis (post-stratification) was conducted to examine the effects of surgery duration on the peri-implant crestal bone loss. Since the results showed no correlation between the two, it was possible to rule out selection bias. More importantly, all the implants used had a similar design and were from the same implant company, and were placed by either one of two board-certified surgeons under the same sterile conditions. Radiographic settings were also the same for all radiographs taken in order to comply with methodology standardization. Moreover, the standardized conditions and the double-masked randomized study design using an identical placebo given at the same frequency and duration as the antibiotics given to the intervention group have protected the study from measurement bias.

One of the limitations of this study is that the results might not be extrapolated to include other types of antibiotics or more complex surgeries involving bone grafting or sinus lift procedures

concomitant with implant placement, or surgeries done by inexperienced operators. Also, the small sample size prevents any generalization in larger populations and could not provide sufficient statistical power to determine the implant survival rate between the two antibiotic regimens. While the inclusion of healthy participants allowed this study to have a homogenous population, the effects of antibiotics on clinical and patient-based outcomes in medically compromised individuals could not be investigated. Another limitation of this study was that the frequency of use of the 0.12% chlorhexidine mouthwash was not registered in the participants' logbook. It was shown in a large clinical study (98) that the perioperative use of a 0.12% chlorhexidine digluconate solution significantly reduced the incidence of postoperative implant complications. The use of a 0.12% chlorhexidine mouthwash should therefore be monitored in the next phase-II clinical trial to ensure standardized postoperative measures. Another limitation of the study was that the presence of pre-existing temporomandibular disorders (TMDs) was not evaluated at baseline. Since several TMDs such as anchored disc phenomenon, irreductible anterior disc displacement and ankylosis are associated with trismus (99), participants could be screened during the initial consultation in the future phase-II trial. Lastly, the quality of the soft tissue around each implant was not assessed. Although the presence of a thin (< 2mm) compared to a thick (≥ 2mm) soft tissue biotype was not associated with peri-implant bone remodeling at one year after implant loading (100), several recent systematic reviews (101-104) reported a keratinized gingiva with a minimal width of 2 mm to maintain peri-implant health . This factor should be taken into consideration in further long-term studies to determine implant success.

4.4 CLINICAL RELEVANCE AND PRACTICAL IMPLICATIONS

This study was the first placebo-controlled double-blinded randomized clinical trial studying the effects of antibiotics on radiographical, clinical and patient-based outcomes after implant surgery. This type of design was aimed at reducing as much as possible the risk of bias and increasing the quality of the evidence. The results of this phase-I randomized clinical trial demonstrated that there were no additional benefits in giving postoperative antibiotics to minimize peri-implant crestal bone remodeling in healthy patients undergoing straightforward platform-switched implant placement. Therefore, a single preoperative dose of antibiotics one hour prior to implant placement may be enough to prevent implant complications since this will involve minimal antibiotic side effects, financial burden and risk of developing antibacterial resistance compared to an additional postoperative antibiotic regimen. This will have to be confirmed in a phase-II clinical trial.

4.5 FUTURE RESEARCH

Bone repair and remodeling after implant placement is a complex, multifactorial surgery that involves several cell types. The effects of antibiotics on the osseointegration process must be addressed. Antibiotics might affect bone healing after implant placement but only in the early phases of bone healing (105) and this should be taken into consideration in future well-controlled *in vivo* and clinical studies.

Since the failure of an implant may cause significant psychological, financial and esthetic consequences to the patient, it is important to control most contributing factors, including perioperative antibiotic usage. Furthermore, the effects of antibiotics on peri-implant bone remodeling, postoperative morbidities and implant survival in medically compromised individuals remain to be explored. Therefore, larger placebo-controlled clinical studies with follow-ups of at least one year are warranted to evaluate the effects of perioperative antibiotics on implant survival as well as patient-based outcomes in both healthy and medically compromised populations.

CHAPTER V

CONCLUSION

The results from this phase-I clinical trial suggest that in healthy patients undergoing uncomplicated platform-switched implant surgery:

- Giving additional antibiotics after implant placement over seven days did not influence peri-implant crestal bone levels after four months.
- Pain severity and postoperative morbidities were not statistically significantly different between the intervention and control groups, except for interfering with daily activities.
- The one-year implant survival rate was 100% in both groups.
- The results of this phase-I clinical trial should be confirmed by a phase-II trial

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APPENDICES

APPENDIX I. CONSENT FORM

Faculté de médecine dentaire

Comparaison de deux différents régimes d'antibiotiques pour la pose d'implant dentaires : une étude clinique randomisée

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- Dr Issam Kersheh, assistant de recherche;
- Dre Nathalie Rei, co-chercheure et spécialiste en médecine buccale;
- Dr René Voyer, co-chercheur et chirurgien;
- Dr Pierre Boudrias, co-chercheur, chirurgien et spécialiste en prosthodontie;
- Dr Simon Tran, co-chercheur
- Mme Marie-Josée Jobin, assistante dentaire et assistante de recherche;

Formulaire d'information et de consentement

Renseignements généraux

Nous vous demandons de participer à ce projet de recherche parce que vous désirez recevoir une restauration sur un ou plusieurs implants. Avant d'accepter de participer à ce projet de recherche, veuillez prendre le temps de comprendre et de considérer attentivement les renseignements qui suivent.

Ce formulaire de consentement vous explique le but de cette étude, les procédures, les avantages, les risques et les inconvénients, de même que les personnes avec qui communiquer au besoin.

Le présent formulaire peut contenir des mots que vous ne comprenez pas. Nous vous invitons à poser toutes les questions que vous jugerez utiles au chercheur et aux autres membres du personnel impliqué dans ce projet de recherche et à leur demander de vous expliquer tout mot ou renseignement qui n'est pas clair.

Si vous désirez participer à l'étude, veuillez contacter notre assistante de recherche, Mme Marie-Josée Jobinau 514 343-6111 poste 3615 afin confirmer votre participation à notre étude et nous rapporter votre formulaire de consentement signé lors du prochain rendez-vous.

Description de l'étude

Les investigateurs veulent déterminer s'il y a une association entre la prise d'antibiotiques avant et/ou après la pose d'implants et le taux de succès des implants, ainsi que la douleur et l'inconfort lors de la phase postopératoire. Ils désirent aussi investiguer s'il y a une association entre deux différents régimes d'antibiotiques et la présence de signes de complications comme l'enflure et l'ecchymose suite à la pose d'implant. Environ 50 hommes et femmes participeront à cette étude et les participants seront divisés au hasard en deux groupes : le premier groupe prendra des antibiotiques avant et après la chirurgie et le deuxième groupe prendra une dose préopératoire et prendra des placébos après la chirurgie qui sont identiques à l'antibiotique sélectionné. Le placébo, dans cette étude, sera une capsule complètement identique à l'antibiotique et contiendra une poudre alimentaire inodore et sans goût particulier. Elle sera prise à la même fréquence que l'antibiotique. Il ne vous sera donc pas possible de deviner le groupe d'étude dans lequel vous vous trouvez.

L'objectif primaire de cette étude est donc de déterminer si donner des antibiotiques pré-opératoirement et post-opératoirement aura un effet significatif sur le degré de perte osseuse au pourtour des implants par rapport à une seule dose pré-opératoire lors de la guérison initiale (3 mois à 1 an). Les objectifs secondaires sont de déterminer la perception des patients par rapport au processus de guérison postopératoire, la perception du chirurgien par

rapport au processus de guérison pour chacun des régimes d'antibiotiques, de déterminer le degré d'inflammation au pourtour des implants lors du processus de guérison et de comparer le taux de survie entre les deux différents régimes. Dans le cas qu'il y ait une association, les chercheurs espèrent déterminer le régime d'antibiotiques idéal à adopter.

Nature et durée de votre participation à cette étude

Si vous vous portez volontaire pour participer à cette étude, les procédures de l'étude se feront en quatre rendez-vous. Le premier rendez-vous comportera une consultation préopératoire pour vous permettre de lire les procédures de l'étude et de bien comprendre et signer le formulaire de consentement éclairé. De plus, les risques associés à la pose d'implants seront discutés en détails. Le deuxième rendez-vous consistera à remplir avec le chirurgien un questionnaire médical et sociodémographique, la prise d'une dose d'antibiotiques préopératoire et la chirurgie implantaire. Une radiographie sera prise une fois l'implant en place. On vous remettra un questionnaire pour que vous puissiez qualifier votre douleur à intervalles réguliers et un journal de bord afin que vous entriez le nombre d'analgésiques et d'antibiotiques pris à chaque jour pour la première semaine postopératoire. De plus, les instructions quant à la façon de prendre l'antibiotique et les analgésiques, ainsi que les conseils postopératoires vous seront remis. Il est important de savoir que votre assignation à un des deux groupes sera sélectionnée au hasard à l'aide d'un système informatique et que ni vous, ni votre chirurgien sera mis au courant du régiment d'antibiotiques que vous prendrez. Le troisième rendez-vous sera planifié une semaine plus tard afin que le chirurgien puisse enlever les sutures et vérifier la guérison initiale. Il remplira un formulaire afin de détecter s'il y a des signes postopératoires comme de l'enflure, une ecchymose, un déchaussement de la gencive ou un exsudat purulent. Il évaluera aussi la présence de plaque et procèdera à la prise d'échantillon de salive au pourtour du/des implant(s) pour mesurer la concentration de certains enzymes qui sont impliqués dans le phénomène de résorption osseuse à l'aide de minuscules bandes de papier qui seront insérées entre la gencive et l'implant. Cette étape d'échantillonnage est habituellement sans douleur. Un quatrième rendez-vous sera fixé, 3 semaines plus tard afin qu'un examinateur vérifier la présence de plaque et procèdera à la prise d'échantillon de salive au pourtour du/des implant(s). Le cinquième rendez-vous, aura lieu 4mois après la pose de/des implant(s) afin qu'un examinateur puisse vérifier la guérison avancée de l'implant et de vérifier s'il est ostéo-intégré et prêt à être restauré par un étudiant. Il prendra une radiographie de l'implant et il l'examinera. Il évaluera également la présence de plaque et procèdera à la prise d'échantillon de salive au pourtour du/des implant(s). Il procèdera aux mêmes procédures que le dentiste ou l'hygiéniste font lors d'un examen dentaire de routine. Ce sera fait afin de mesurer la profondeur de l'espace entre votre implant et votre gencive et pour voir si vos gencives saignent lorsqu'elles sont examinées. Vous serez peut-être un peu inconfortable et aurez un peu de saignement des gencives si elles sont enflées. Cet inconfort devrait être temporaire et disparaitra dans les minutes suivant l'examen. Nous vous contacterons 1 an après la pose de l'implant pour prendre une dernière radiographie à chaque rendez-vous afin de vérifier la progression de la guérison osseuse de l'implant.

Conditions de participation

Vous pouvez participer à cette étude si :

- Vous avez une gencive relativement en bonne santé et que votre hygiène buccodentaire est bonne.
- Vous êtes partiellement édenté et vous désirez remplacer une ou plusieurs dents manquantes par une couronne ou un pont fixe sur implants.

- Vous présentez un volume osseux et gingival pouvant recevoir la pose d'un implant sans avoir recourt à une greffe osseuse ou gingivale lors de la chirurgie.
- Vous pouvez donner votre consentement écrit et suivre toutes les procédures de l'étude.

Vous ne pouvez pas participer à cette étude si:

- Vous prenez de façon régulière des analgésiques ou des antidépresseurs.
- Vous avez une infection buccale non traitée incluant la parodontite.
- Vous fumez 10 cigarettes/cigares ou plus par jours.
- Vous consommez des substances illicites.
- Vous êtes complètement édenté.
- Vous êtes enceinte ou vous allaitez.
- Vous êtes allergique à la pénicilline, à la céphalosporine (ex. : Suprax®, Keflex®), ou aux anti-inflammatoires non stéroïdiens (ex. : Aspirin®, Advil®, Motrin®).
- Vous avez ou êtes susceptibles à faire des ulcères d'estomac.
- Vous êtes atteint d'une immunodéficience locale ou systémique.
- Vous êtes atteint de diabète ou toute autre maladie systémique non contrôlée.
- Vous êtes atteint de dyscrasie sanguine affectant la coagulation.
- Vous avez reçu des traitements de radiothérapie dans la région de la tête et du cou.
- Vous prenez des bisphosphonates oraux (ex. : Fosamax®, Actonel®, Boniva®) depuis plus de 3 ans ou prenez des bisphosphonates intraveineux (ex. : Reclast®).
- Vous prenez des corticostéroïdes (ex. : prednisone, cortisone, Decadron®, Medrol®) depuis plusieurs années.
- Vous devez prendre des antibiotiques avant de recevoir des traitements dentaires.

Risques et inconforts

Après l'examen des gencives qui se fera 4 mois plus tard, il se pourrait que vous ressentiez un léger inconfort. Pour diminuer votre inconfort, vous pouvez demander l'application d'un gel topique pour anesthésier ou « engourdir » vos gencives. Les effets secondaires suivants peuvent être reliés à la prise de l'amoxicilline (antibiotique) : nausée, vomissements, diarrhée, éruption cutanée et urticaire. Les effets secondaires plus rares sont le saignement prolongé, et l'enflure de la langue, des gencives et des joues.

Les effets secondaires qui peuvent être reliés à la prise de l'ibuprofène sont les suivants :
- Nausée, maux d'estomac (dans 3 à 9% des cas).
- Vomissements, diarrhée, constipation, douleurs abdominales ou crampes, indigestion, flatulence, enflure abdominale (dans 1 à 3% des cas).
- Ulcères d'estomac ou intestinales, saignement gastro-intestinal ou annal, hépatite, jaunisse, fonction du foie anormale (moins de 1% des cas).
- Étourdissements (3 à 9% des cas).
- Maux de tête, nervosité (1 à 3% des cas).
- Dépression, insomnie (moins de 1% des cas).
- Certains ont rapporté des paresthésies (perte de sensation localisée), hallucinations et avoir fait des « rêves étranges ».
- Acouphènes (1 à 3% des cas).
- Vision brouillée ou diminuée, champs de vision diminué, changements de couleur, conjonctivite (moins de 1% des cas).
- Éruption cutanée (3 à 9% des cas).
- Démangeaisons (1 à 3% des cas).

- Éruptions vésiculo-bulleuses, urticaires (moins de 1% des cas).
- Enflure des extrémités (1 à 3% des cas).
- Polyurie (uriner souvent), fièvre (très rare).

Il est important de noter que l'ibuprofène peut aussi augmenter le temps de saignement mais à un taux généralement moins important que l'aspirine.

Les effets secondaires communs reliés à la prise de l'acétaminophène sont la nausée, l'éruption cutanée et les maux de tête. Les effets secondaires plus rares sont le saignement prolongé, saignement du nez, et urticaire.

Si vous dénotez un des effets secondaires énumérés ci-dessus, veuillez contacter immédiatement le chercheur principal, Dr. Robert Durand, au (514) 343-7464. En cas d'absence, vous pouvez contacter le Dr. René Voyer, co-chercheur, au (514) 343-5926.

Si vous dénotez une éruption cutanée, et/ou de l'urticaire, une situation qui peut survenir relativement fréquemment dans la population en général, veuillez discontinuer immédiatement la prise de l'amoxicilline et de l'ibuprofène et contacter le chercheur principal, Dr. Robert Durand, au (514) 343-7464 ou le Dr. René Voyer au (514) 343-5926. Le choc anaphylactique (réaction allergique sévère) est l'effet secondaire le plus grave et consiste en l'enflure des voies respiratoires, notamment du cou et de la gorge. Les individus, dans cette situation qui peut être fatale, éprouveront de la difficulté à respirer. Si cette situation survient, vous devrez immédiatement contacter le 9-1-1 et vous devrez en informer le personnel de recherche lors de votre prochaine visite.

Si vous êtes si inconfortable et que vous désirez vous retirer de l'étude, vous pouvez le faire sans pénalité. Si vous avez un inconfort qui vous dérange le chercheur principal,
Dr. Robert Durand, à la Faculté de médecine dentaire de l'Université de Montréal au (514) 343-7464. Les chercheurs rapporteront les effets secondaires au comité d'éthique à la recherche de l'Université de Montréal.

Avantages à participer

Les résultats obtenus vont contribuer à l'avancement des connaissances dans le domaine de l'implantologie dentaire quant au régime d'antibiotiques à adopter pour augmenter les chances de succès des implants et diminuer l'incidence des complications postopératoires.

Compensation et indemnisation

Vous recevrez une compensation financière de 100.00$ pour votre participation à ce projet de recherche.

En signant le présent formulaire d'information et de consentement, vous ne renoncez à aucun de vos droits ni ne libérez les chercheurs, ni l'établissement de leurs responsabilités civiles ou professionnelles. Si vous deviez subir un préjudice ou quelque lésion que ce soit du à votre participation à ce projet (i.e. résultat des procédures), vous recevrez tous les soins et services requis par l'état de votre santé, sans frais de votre part.

Diffusion des résultats

Vous pourrez communiquer avec l'équipe de recherche afin d'obtenir de l'information sur l'avancement des travaux ou les résultats du projet de recherche. Si vous désirez connaitre les résultats de nos travaux, veuillez nous laisser votre adresse courriel et ils vous seront envoyés par courriel, après qu'ils auront été publiés dans un journal scientifique.

Protection de la confidentialité
Durant votre participation à ce projet, le chercheur et son équipe recueilleront dans un dossier de recherche les renseignements vous concernant nécessaires pour répondre aux objectifs scientifiques.
Tous les renseignements recueillis demeureront strictement confidentiels. Étant donné que les numéros de dossier de chaque participant sera écrit sur les questionnaires et les feuilles de données cliniques, une tierce personne (assistant(e) de recherche) enlèvera ces numéros de dossiers avant que ces documents ne soient analysés et les remplacera par un code secret. La clé du code, reliant votre nom à votre dossier de recherche, sera conservée par cette tierce personne dans un local fermé à clé où seule cette dernière aura accès.

Les informations personnelles, cliniques, et les résultats de la recherche recueillis seront conservés dans un dossier de recherche spécifiquement conçu pour le projet de recherche. Les données de recherche seront conservées pendant sept ans après la fin de l'étude et seront détruites par la suite.

Vous avez le droit de consulter votre dossier de recherche pour vérifier les renseignements recueillis, et les faire rectifier au besoin, et ce, aussi longtemps que le chercheur responsable du projet ou l'établissement détiennent ces informations. Cependant, afin de préserver l'intégrité scientifique du projet, vous pourriez n'avoir accès à certaines de ces informations qu'une fois votre participation terminée.

Pour des raisons de surveillance et de contrôle de la recherche, votre dossier de recherche ainsi que votre dossier dentaire pourront être consultés par une personne mandatée par le Comité d'éthique de la recherche en santé (CERES) de l'Université de Montréal. Toutes ces personnes respecteront la politique de confidentialité. Les données pourront être publiées dans des revues scientifiques, mais il ne sera pas possible de vous identifier.

Participation volontaire et possibilités de retrait
Votre participation à ce projet est tout à fait volontaire. Vous êtes donc libre de refuser d'y participer sans que cela n'affecte la qualité des soins dentaire que vous recevrez en tant que patient à la clinique de la Faculté de Médecine Dentaire. Vous pouvez également vous retirer de l'étude à n'importe quel moment sans donner de raison. Vous avez simplement à aviser le chercheur responsable du projet ou l'un des membres de l'équipe.

Le chercheur responsable du projet de recherche peut aussi mettre fin à votre participation si vous ne respectez pas les consignes du projet de recherche ou si cela n'est plus dans votre intérêt. Par ailleurs, le Comité d'éthique de la recherche en santé (CERES) de l'Université de Montréal peut également mettre fin au projet, notamment pour des raisons de sécurité ou de faisabilité. En cas de retrait ou d'exclusion, les renseignements qui auront été recueillis au moment de votre retrait seront détruits.

Responsabilité de l'équipe de recherche
En acceptant de participer à cette étude, vous ne renoncez à aucun de vos droits ni ne libérez les chercheurs, le commanditaire ou l'établissement de leurs responsabilités civiles et professionnelles.

Personnes-ressources
Si vous avez des questions au sujet de cette étude, vous pouvez communiquer (avant, pendant et après l'étude) avec une des personnes suivantes :

- Dr Robert Durand au 514-343-7464 entre 9h00 et 17h00
- En cas d'urgence médicale, communiquer avec le 9-1-1 ou encore avec le service d'urgence de l'Université de Montréal au 514-343-7771.

Pour toute information d'ordre éthique concernant les conditions dans lesquelles se déroule votre participation à ce projet, vous pouvez contacter la coordonnatrice du Comité d'éthique de la recherche en santé (CERES) par courriel : ceres@umontreal.ca ou par téléphone au (514) 343-6111 poste 2604.

Pour plus d'information sur vos droits comme participants, vous pouvez consulter le portail des participants de l'Université de Montréal à l'adresse suivante : http://recherche.umontreal.ca/participants.

Toute plainte relative à votre participation à cette recherche peut être adressée à l'ombudsman de l'Université de Montréal, au numéro de téléphone (514) 343-2100 ou à l'adresse courriel ombudsman@umontreal.ca. L'ombudsman accepte les appels à frais virés. Il s'exprime en français et en anglais et prend les appels entre 9h et 17h.

Le Comité d'éthique de la recherche en santé de l'Université de Montréal a approuvé ce projet de recherche et en assure le suivi. De plus, il approuvera toute modification apportée au formulaire d'information et de consentement et au protocole de recherche.

Consentement

Votre participation à cette étude est tout à fait volontaire. Vous êtes donc libre d'accepter ou de refuser d'y participer sans que cela n'affecte la qualité de vos traitements à l'Université.

« J'ai pris connaissance du formulaire d'information et de consentement. Je reconnais qu'on m'a expliqué le projet, qu'on a répondu à mes questions à ma satisfaction et qu'on m'a laissé le temps voulu pour prendre une décision. Je consens à participer à ce projet de recherche aux conditions qui y sont énoncées. Une copie signée et datée du présent formulaire d'information et de consentement me sera remise. »

Nom (en lettres moulées) et signature du participant :

Nom : _____

Signature : _____ *Date :*_____

Engagement et signature du chercheur :

« Je certifie qu'on a expliqué au participant les termes du présent formulaire d'information et de consentement, que l'on a répondu aux questions que le participant avait à cet égard et qu'on lui a clairement indiqué qu'il demeure libre de mettre un terme à sa participation, et ce, sans aucune conséquence négative. »

« Je m'engage avec l'équipe de recherche à respecter ce qui a été convenu au formulaire d'information et de consentement et à en remettre une copie signée au participant. »

Nom (en lettres moulées) et signature du chercheur responsable du projet de recherche :

Nom : _____

Signature : _____ *Date :*_____

Signature de la personne qui a obtenu le consentement si différente du chercheur responsable du projet de recherche :

« J'ai expliqué au participant les termes du présent formulaire d'information et de consentement et j'ai répondu aux questions qu'il m'a posées. »

Nom (en lettres moulées) et signature de la personne qui obtient le consentement :

Nom : _____

Signature : _____ *Date :*_____

APPENDIX II. TIMELINE OF RESEARCH APPOINTMENTS

1st– Consultation, selection and consent form given to participants to take home or reviewed and signed with participants.

2nd– Collect medical and sociodemographic questionnaires. Allocation of antibiotic regimen one hour before surgery. Surgery parameters are noted (#implants, specifications of implants, incision length, duration) immediately after surgery. Baseline standardized periapical radiograph is taken. Postoperative instructions and questionnaires on pain and interference with daily activities are given to participants. Envelopes are given with randomly pre-selected antibiotic regimen to take postoperatively.

3rd– One-week postoperative control to verify initial healing. Questionnaires are collected and clinical data is collected for bruising, swelling, suppuration and wound dehiscence. Modified plaque index is measured.

4th– Three-week postoperative control, modified plaque index is measured.

5th– Four-month postoperative control and impressions for implant-supported prosthesis as planned in patient's initial treatment plan. Clinical and radiographic exams are executed to assess implant status (osseointegration: yes/no, presence of complications). A standardized radiograph is taken. The modified plaque index is measured.

6th– One year later, a radiograph is taken and the implants are clinically examined.

APPENDIX III. MEDICAL QUESTIONNAIRE

HISTOIRE MÉDICALE (ADDENDUM) POUR LE PROJET DE RECHERCHE INTITULÉ :

Comparaison de deux différents régimes d'antibiotiques pour la pose d'implant dentaires : une étude clinique randomisée

Date: / /
a a m m j j

No. de dossier / Code d'identification

Sexe: ☐M ☐ F

Date de naissance:

/ /
a a m m j j

Histoire dentaire

Devez-vous prendre des antibiotiques avant de recevoir des traitements dentaires?

☐ OUI
☐ NON

Histoire médicale

Avez-vous pris des médicaments durant les 3 derniers mois? ☐ OUI
☐ NON

Si oui, lesquels? _____

Êtes-vous allergiques à un ou plusieurs médicaments? ☐ OUI
☐ NON

Si oui, lesquels? _____

Faites-vous du diabète? ☐ OUI

☐ NON

Si oui, quel type de diabète?: I ☐ II ☐

Utilisez-vous du tabac présentement?	○ Oui, _____ cigarettes par jour ○ Oui, _____ cigares par jour ○ Oui, _____ autre forme de tabac par jour	○ Non
Si vous n'utilisez pas du tabac présentement, avez-vous déjà utilisé du tabac?	○ Oui, dans les derniers 6 mois ○ Oui, dans la dernière année ○ Oui, il y a de 1 à 2 ans ○ Oui, il y a de 2 à 5 ans ○ Oui, il y a de 5 à 8 ans ○ Oui, il y a 10 ans et plus	○ Non
Si oui,	○ Oui, _____ cigarettes par jour ○ Oui, _____ cigares par jour ○ Oui, _____ autre forme de tabac par jour	

APPENDIX IV. SOCIODEMOGRAPHIC QUESTIONNAIRE

INFORMATIONS SOCIODÉMOGRAPHIQUES pour projet de recherche intitulé:

Comparaison de deux différents régimes d'antibiotiques pour la pose d'implant dentaires : une étude clinique randomisée

Date : _____

/ /

a a m m j j

No. de dossier/ Code d'identification :

Prière de répondre aux questions suivantes.

Sexe : ○ Masculin ○ Féminin

Langue maternelle : ○ Français ○ Anglais ○ Allemand ○ Espagnol ○ Autre :

Dans quel pays êtes-vous né? _____

Les personnes qui vivent au Canada proviennent de plusieurs milieux culturels et géo ethniques différents. Quel est votre parcours culturel et géo ethnique? Veuillez cocher tout ce qui s'applique à vous :

○ Africain (Afrique / Afro-américain)

○ Amérique du Nord / Canadien-Français / Mexique (ex. : Américain, Canadien, Mexicain)

○ Asie de l'Est : Veuillez en cocher SVP :

○ Chinois ○ Philipin

○ Japonais ○ Coréen

○ Amérique du Sud et Centrale (Américain Latine / Hispano-américain)

○ Européen (ex. : Slave, Germanique, Scandinave, Anglo-Saxon, Français, Grecque)

○ Autochtones / Natif Américain

○ Moyen-Orient / Afrique du Nord (ex. : Afgan, Égyptien, Algérien, Iranien, Irakien, Syrien, Libanais, Turc)

○ Asie du Sud (ex. : Indien, Pakistanais, Sri Lankais)

○ Asie du Sud-Est (ex. : Cambodgien, Indonésien, Laotien, Vietnamien)

En vous référant à la liste ci-dessus, quelle est l'origine culturelle et géo ethnique de vos parents?

Mère? _____

Père? _____

État civil : ○ Célibataire ○ Marié(e) ○ Séparé(e) ○ Divorcé(e) ○ Veuf(ve) ○ Je préfère ne pas répondre

Vous vivez… ○ Seul(e)? ○ En famille? ○ Avec d'autres adultes?

Niveau de scolarité : ○ Primaire (7 ans et moins) ○ Secondaire (8-12 ans) ○ Collège (13-15 ans) ○ Université (16 ans et plus)

Emploi actuel : ○ À temps complet ○ À temps partiel ○ Au foyer ○ Étudiant(e)

		○ En chômage	○ Retraité(e)
Revenu annuel :	familial	○ Moins de 19 999$	○ Entre 20 000 et 29 999$
		○ Entre 30 000 et 39 999$	○ Entre 40 000 et 49 999$
		○ Entre 50 000 et 59 999$	○ Entre 60 000 et 74 999$
		○ Plus de 75 000$	

APPENDIX V. POSTOPERATIVE INSTRUCTIONS

INSTRUCTIONS POSTOPÉRATOIRES

Les informations qui suivent ont été préparées pour répondre à vos questions sur la façon de remplir correctement le questionnaire, mais aussi prendre soin de votre bouche suite à la chirurgie implantaire. Veuillez en prendre connaissance attentivement.

Un analgésique (ibuprofène) vous a été prescrit dans le but de soulager votre inconfort Cette médication peut être irritante pour l'estomac si bien qu'il est recommandé de l'ingérer avec de la nourriture. Vous devez prendre un comprimé **tous les quatre heures** jusqu'au coucher. À votre réveil le lendemain matin, veuillez prendre un comprimé et à partir de ce moment le médicament doit à nouveau être pris à intervalle de quatre heures jusqu'au coucher. Cette procédure est à respecter rigoureusement **pendant les premières quarante-huit heures suivant la chirurgie**, à la suite de quoi, vous pourrez prendre le médicament seulement lorsque que vous le jugerez nécessaire. **Veuillez noter dans le questionnaire à l'endroit prévu à cet effet l'heure à laquelle chacun des comprimés est pris.** Si vous devez utiliser la médication de secours (acétaminophène), assurez vous d'attendre au moins deux heures après avoir pris la médication principale. Pour la médication de secours comme pour la médication principale, veuillez inscrire la date et l'heure auxquelles vous l'avez pris. Vous ne devrez prendre qu'un seul comprimé de la médication de secours. Par contre, si après deux heures vous ne ressentez toujours pas de soulagement, vous pourrez en prendre un autre. Vous pourrez prendre jusqu'à un maximum de huit comprimés par jour de médication de secours, c'est-à-dire à un intervalle minimum de trois heures. Cependant, assurez vous de toujours continuer à prendre la médication principale à l'intervalle prescrit.

Dans les premières quarante-huit heures suivant la chirurgie, il est préférable de ne pas consommer de liquide chaud. Les aliments mous et coupés en petits morceaux doivent être privilégiés. Il faut éviter les agrumes ou les jus de fruits, la nourriture épicée et les breuvages alcoolisés.

Lors des six premières semaines, il faut tenter de mastiquer les aliments de consistance plus dure (ex. : légumes crus, pain croûté, pommes) du côté qui na pas été opéré afin d'éviter la pression sur l'implant, à moins d'avis contraire de la part de votre chirurgien.

Il est important de ne pas fumer. La chaleur et la fumée irriteront vos gencives et les effets secondaires de la nicotine vont retarder la guérison.

Lors du brossage, il ne faut pas brosser le pansement et il faut brosser doucement au niveau des dents de la région opérée. La soie dentaire quant à elle ne peut pas être passée entre les dents concernées par la chirurgie pour une période d'une semaine. Après le brossage, rincez-vous la bouche matin et soir avec l'équivalent d'un bouchon du rince-bouche prescrit

(gluconate de chlorhexidine 0,12%) pendant une minute. L'ordonnance pour ce rince-bouche vous a été remise en même temps que les comprimés.

Au courant de la première journée, appliquer de façon intermittente selon un intervalle de vingt minutes de la glace sur votre visage dans la région opérée. Ceci a pour but de minimiser l'inflammation et l'enflure.

Vous pouvez poursuivre vos activités quotidiennes, mais il est préférable de ne pratiquer aucun sport et d'éviter les efforts physiques intenses pour les premières quarante-huit heures après la chirurgie.

L'enflure est normale et elle débute habituellement un à deux jours après la chirurgie pour ensuite disparaître trois à quatre jours après. Si l'enflure est douloureuse ou semble empirer, veuillez nous contacter.

Du sang peut être présent dans la salive jusqu'à vingt-quatre heures après l'opération. Ce n'est pas anormal et la situation devrait se corriger d'elle-même. Si le saignement persiste, prenez un morceau de gaze ou un sac de thé humidifié et appliquez de la pression sur le pansement pendant une vingtaine de minutes. Si le saignement ne s'est pas arrêté au bout des vingt minutes, veuillez nous contacter.

Si d'autres problèmes se produisent ou vous avez des questions ou des inquiétudes, n'hésitez pas à entrer en contact avec nous.

Dr René Voyer : 514 343-5926
Dr Robert Durand : 514 343-7464

APPENDIX VI. PAIN AND INTERFERENCE WITH DAILY ACTIVITIES QUESTIONNAIRE

QUESTIONNAIRE D'ÉVALUATION DE LA DOULEUR ET DE L'INCONFORT

Pour projet intitulé « Comparaison de deux différents régimes d'antibiotiques pour la pose d'implant dentaires : une étude clinique randomisée »

*No. dossier / Code d'identification :*_____

(À l'usage du personnel de recherche seulement)

Nom, Prénom : _____

Date : _____

JOURNAL DE BORD

JOUR 1 – JOUR DE L'INTERVENTION

Prises d'analgésiques :

Veuillez noter ci-dessous l'heure à laquelle vous prenez chacun de vos comprimés d'ibuprofène. Veuillez aussi noter si vous avez pris la médication de secours.

Premier comprimé : _____
Deuxième comprimé : _____
Troisième comprimé : _____

Quatrième comprimé : _____

Avez-vous fait usage de la médication de secours ? _____

Si oui, à quel moment? Heure : _____Quantité :_____

Heure : _____Quantité :_____

Heure : _____Quantité :_____

Heure : _____Quantité :_____

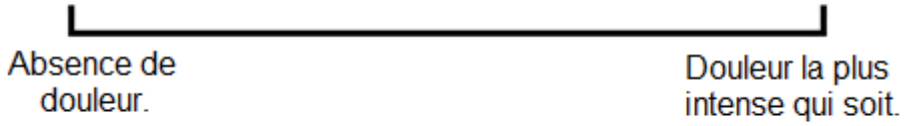
Heure : _____Quantité :_____

Évaluation de la douleur:

Sur les échelles visuelles ci-dessous, vous devez quantifier l'intensité de votre douleur à chaque heure en prenant soin de noter l'heure correspondante jusqu'à l'heure du coucher. Il s'agit dans un premier temps de marquer un trait vertical sur la ligne à l'endroit qui convient selon vous à la douleur que vous ressentez. Vous devez ensuite attribuer à cette même douleur une note qui se situe entre zéro et dix, zéro représentant l'absence de douleur et dix la douleur la plus intense qui soit.

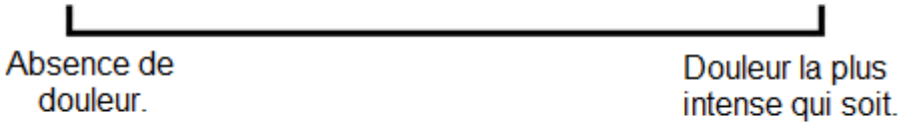
Jour de l'intervention (Jour 1)

- Immédiatement après la chirurgie : Heure :_____



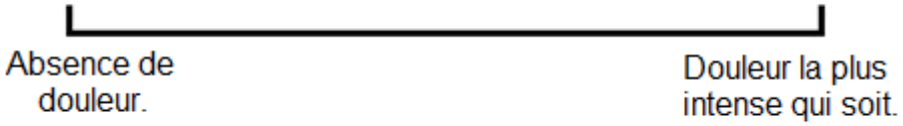
Note : _____

- 20 minutes après la chirurgie : Heure :_____



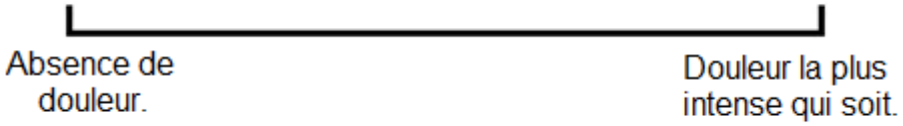
Note : _____

- 40 minutes après la chirurgie : Heure :_____



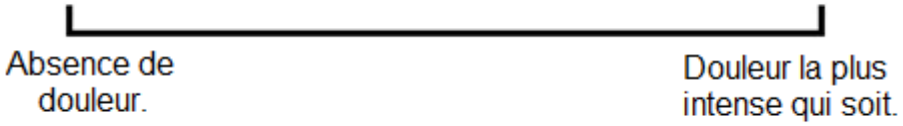
Note : _____

- 1 heure après la chirurgie : Heure :_____



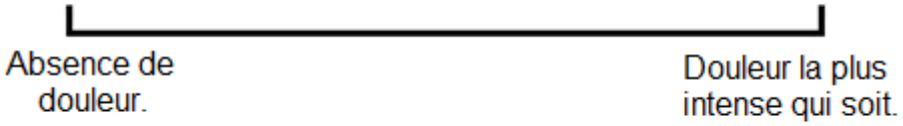
Note : _____

- 2 heures après la chirurgie : Heure :_____



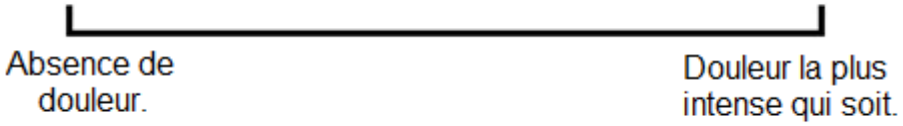
Note : _____

- 3 heures après la chirurgie : Heure :_____



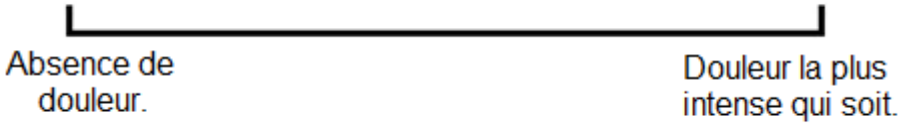
Note : _____

- 4 heures après la chirurgie : Heure :_____



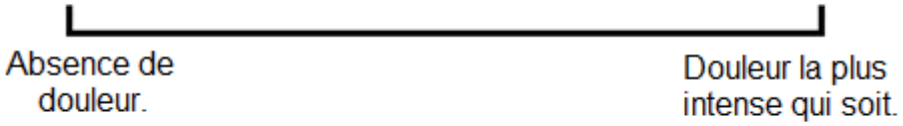
Note : _____

- 5 heures après la chirurgie : Heure :_____



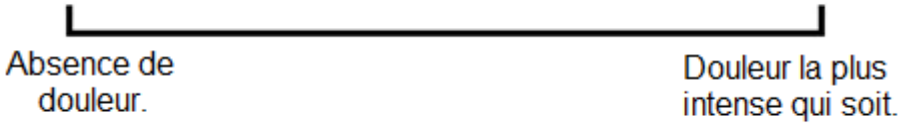
Note : _____

- 6 heures après la chirurgie : Heure :_____



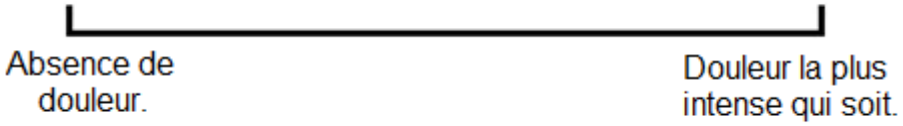
Note : _____

- 7 heures après la chirurgie : Heure :_____



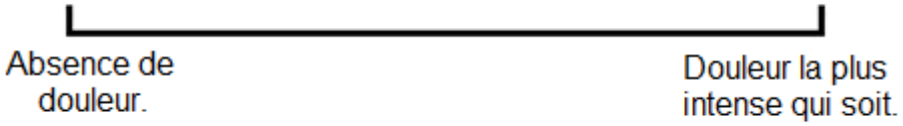
Note : _____

- 8 heures après la chirurgie : Heure :_____



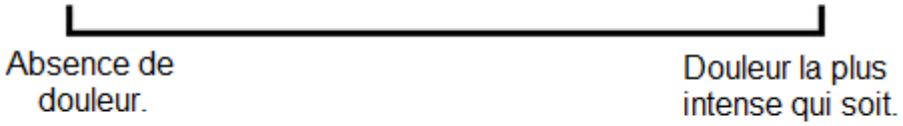
Note : _____

- 9 heures après la chirurgie : Heure :_____



Note : _____

- 10 heures après la chirurgie : Heure :_____



Note : _____

- 11 heures après la chirurgie : Heure :_____

Absence de douleur. Douleur la plus intense qui soit.

Note : _____

- 12 heures après la chirurgie : Heure :_____

Absence de douleur. Douleur la plus intense qui soit.

Note : _____

<u>Interférences avec les activités quotidiennes :</u>

Sur les échelles visuelles ci-dessous, vous devez quantifier une fois par jour seulement l'intensité avec laquelle la chirurgie interfère avec vos activités quotidiennes en prenant soin de noter l'heure correspondante.

- Jour de l'intervention (Jour 1): Heure :_____

Est-ce que la chirurgie interfère avec votre capacité à mastiquer les aliments de votre choix ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à ouvrir grand la bouche ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à parler ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à dormir ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à aller au travail ou à l'école ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à mener une vie sociale normale ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à participer à votre activité récréative préférée ?

Pas du tout Extrêmement

JOUR 2

Prises d'analgésiques :

Veuillez noter ci-dessous l'heure à laquelle vous prenez chacun de vos comprimés d'ibuprofène. Veuillez aussi noter si vous avez pris la médication de secours.

Premier comprimé : _____
Deuxième comprimé : _____
Troisième comprimé : _____
Quatrième comprimé : _____
Avez-vous fait usage de la médication de secours ? _____

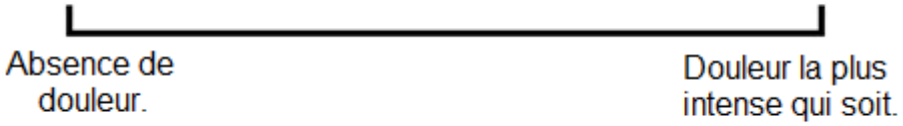
Si oui, à quel moment? Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____

Évaluation de la douleur:

Sur les échelles visuelles ci-dessous, vous devez quantifier l'intensité de votre douleur à chaque heure en prenant soin de noter l'heure correspondante jusqu'à l'heure du coucher. Il s'agit dans un premier temps de marquer un trait vertical sur la ligne à l'endroit qui convient selon vous à la douleur que vous ressentez. Vous devez ensuite attribuer à cette même douleur une note qui se situe entre zéro et dix, zéro représentant l'absence de douleur et dix la douleur la plus intense qui soit.

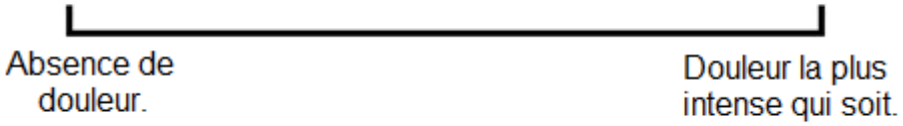
Jour 2.

- Au réveil : Heure :_____



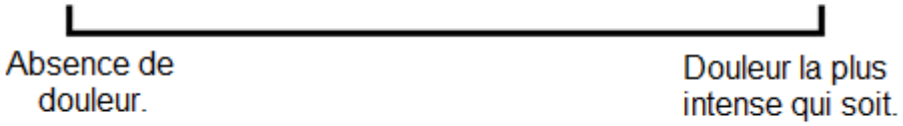
Note : _____

- À midi : Heure :_____



Note : _____

- Au coucher : Heure :_____



Note : _____

Interférences avec les activités quotidiennes :

Sur les échelles visuelles ci-dessous, vous devez quantifier une fois par jour seulement l'intensité avec laquelle la chirurgie interfère avec vos activités quotidiennes en prenant soin de noter l'heure correspondante.

- Jour 2: Heure :_____

Est-ce que la chirurgie interfère avec votre capacité à mastiquer les aliments de votre choix ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à ouvrir grand la bouche ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à parler ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à dormir ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à aller au travail ou à l'école ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à mener une vie sociale normale ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à participer à votre activité récréative préférée ?

Pas du tout Extrêmement

JOUR 3

Prises d'analgésiques :

Veuillez noter ci-dessous l'heure à laquelle vous prenez chacun de vos comprimés d'ibuprofène. Veuillez aussi noter si vous avez pris la médication de secours.

Premier comprimé : _____
Deuxième comprimé : _____
Troisième comprimé : _____
Quatrième comprimé : _____
Avez-vous fait usage de la médication de secours ? _____

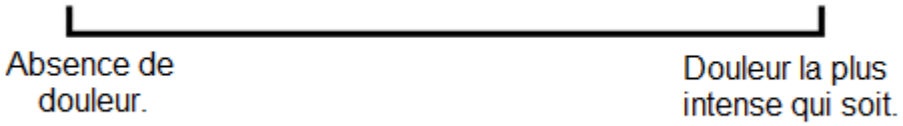
Si oui, à quel moment? Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____

Évaluation de la douleur:

Sur les échelles visuelles ci-dessous, vous devez quantifier l'intensité de votre douleur à chaque heure en prenant soin de noter l'heure correspondante jusqu'à l'heure du coucher. Il s'agit dans un premier temps de marquer un trait vertical sur la ligne à l'endroit qui convient selon vous à la douleur que vous ressentez. Vous devez ensuite attribuer à cette même douleur une note qui se situe entre zéro et dix, zéro représentant l'absence de douleur et dix la douleur la plus intense qui soit.

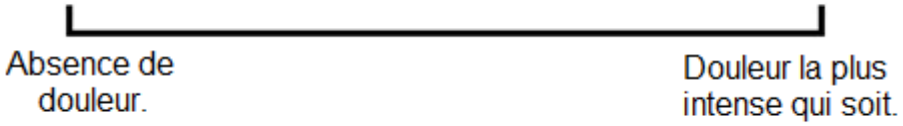
Jour 3.

- Au réveil : Heure :_____



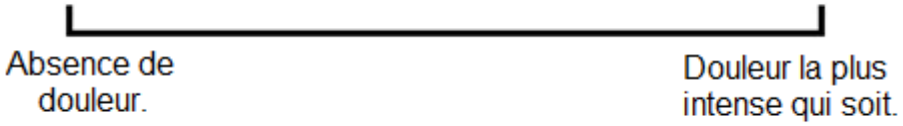
Note : _____

- À midi : Heure :_____



Note : _____

- Au coucher : Heure :_____



Note : _____

<u>Interférences avec les activités quotidiennes :</u>

Sur les échelles visuelles ci-dessous, vous devez quantifier une fois par jour seulement l'intensité avec laquelle la chirurgie interfère avec vos activités quotidiennes en prenant soin de noter l'heure correspondante.

- Jour 3: Heure :_____

Est-ce que la chirurgie interfère avec votre capacité à mastiquer les aliments de votre choix ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à ouvrir grand la bouche ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à parler ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à dormir ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à aller au travail ou à l'école ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à mener une vie sociale normale ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à participer à votre activité récréative préférée ?

Pas du tout Extrêmement

JOUR 4

Prises d'analgésiques :

Veuillez noter ci-dessous l'heure à laquelle vous prenez chacun de vos comprimés d'ibuprofène. Veuillez aussi noter si vous avez pris la médication de secours.

Premier comprimé : _____
Deuxième comprimé : _____
Troisième comprimé : _____
Quatrième comprimé : _____
Avez-vous fait usage de la médication de secours ? _____

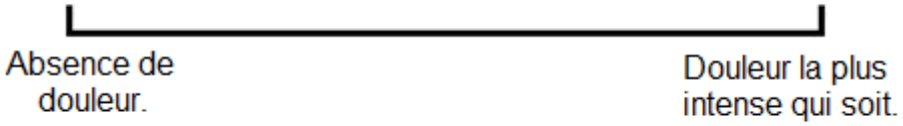
Si oui, à quel moment? Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____

Évaluation de la douleur:

Sur les échelles visuelles ci-dessous, vous devez quantifier l'intensité de votre douleur à chaque heure en prenant soin de noter l'heure correspondante jusqu'à l'heure du coucher. Il s'agit dans un premier temps de marquer un trait vertical sur la ligne à l'endroit qui convient selon vous à la douleur que vous ressentez. Vous devez ensuite attribuer à cette même douleur une note qui se situe entre zéro et dix, zéro représentant l'absence de douleur et dix la douleur la plus intense qui soit.

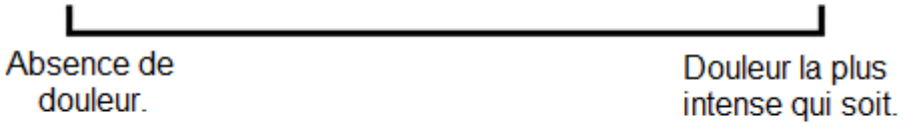
Jour 4.

- Au réveil: Heure :_____



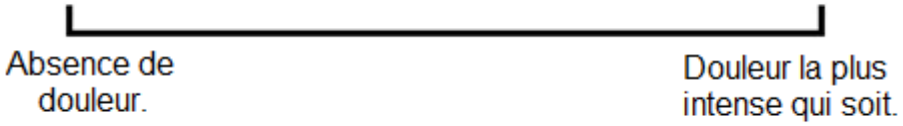
Note : _____

- À midi : Heure :_____



Note : _____

- Au coucher : Heure :_____



Note : _____

<u>Interférences avec les activités quotidiennes :</u>

Sur les échelles visuelles ci-dessous, vous devez quantifier une fois par jour seulement l'intensité avec laquelle la chirurgie interfère avec vos activités quotidiennes en prenant soin de noter l'heure correspondante.

- Jour 4: Heure :_____

Est-ce que la chirurgie interfère avec votre capacité à mastiquer les aliments de votre choix ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à ouvrir grand la bouche ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à parler ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à dormir ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à aller au travail ou à l'école ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à mener une vie sociale normale ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à participer à votre activité récréative préférée ?

Pas du tout Extrêmement

JOUR 5

Prises d'analgésiques :

Veuillez noter ci-dessous l'heure à laquelle vous prenez chacun de vos comprimés d'ibuprofène. Veuillez aussi noter si vous avez pris la médication de secours.

Premier comprimé : _____
Deuxième comprimé : _____
Troisième comprimé : _____
Quatrième comprimé : _____
Avez-vous fait usage de la médication de secours ? _____

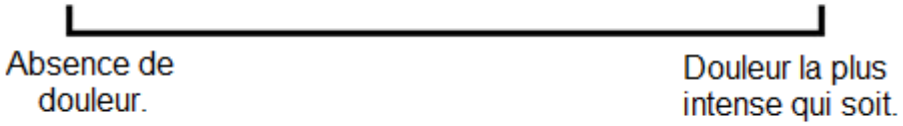
Si oui, à quel moment? Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____

Évaluation de la douleur:

Sur les échelles visuelles ci-dessous, vous devez quantifier l'intensité de votre douleur à chaque heure en prenant soin de noter l'heure correspondante jusqu'à l'heure du coucher. Il s'agit dans un premier temps de marquer un trait vertical sur la ligne à l'endroit qui convient selon vous à la douleur que vous ressentez. Vous devez ensuite attribuer à cette même douleur une note qui se situe entre zéro et dix, zéro représentant l'absence de douleur et dix la douleur la plus intense qui soit.

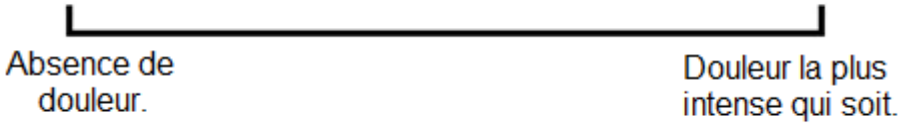
Jour 5.

- Au réveil: Heure :_____



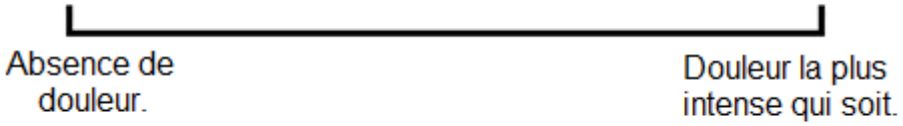
Note : _____

- À midi : Heure :_____



Note : _____

- Au coucher : Heure :_____



Note : _____

<u>Interférences avec les activités quotidiennes :</u>

Sur les échelles visuelles ci-dessous, vous devez quantifier une fois par jour seulement l'intensité avec laquelle la chirurgie interfère avec vos activités quotidiennes en prenant soin de noter l'heure correspondante.

- Jour 5: Heure :_____

Est-ce que la chirurgie interfère avec votre capacité à mastiquer les aliments de votre choix ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à ouvrir grand la bouche ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à parler ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à dormir ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à aller au travail ou à l'école ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à mener une vie sociale normale ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à participer à votre activité récréative préférée ?

Pas du tout Extrêmement

JOUR 6

Prises d'analgésiques :

Veuillez noter ci-dessous l'heure à laquelle vous prenez chacun de vos comprimés d'ibuprofène. Veuillez aussi noter si vous avez pris la médication de secours.

Premier comprimé : _____
Deuxième comprimé : _____
Troisième comprimé : _____
Quatrième comprimé : _____
Avez-vous fait usage de la médication de secours ? _____

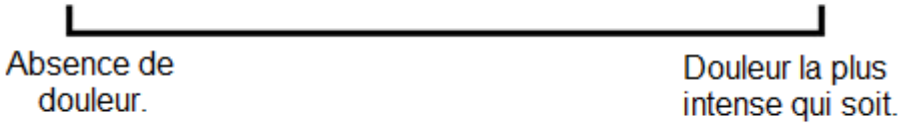
Si oui, à quel moment? Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____

Évaluation de la douleur:

Sur les échelles visuelles ci-dessous, vous devez quantifier l'intensité de votre douleur à chaque heure en prenant soin de noter l'heure correspondante jusqu'à l'heure du coucher. Il s'agit dans un premier temps de marquer un trait vertical sur la ligne à l'endroit qui convient selon vous à la douleur que vous ressentez. Vous devez ensuite attribuer à cette même douleur une note qui se situe entre zéro et dix, zéro représentant l'absence de douleur et dix la douleur la plus intense qui soit.

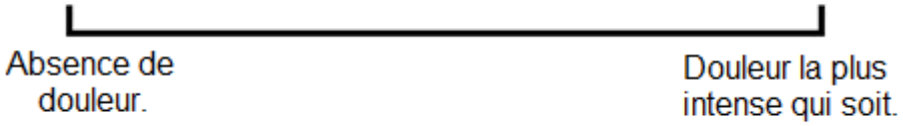
Jour 6.

- Au réveil: Heure :_____



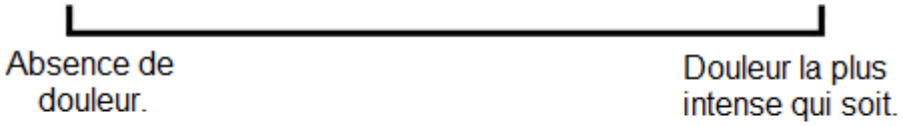
Note : _____

- À midi : Heure :_____



Note : _____

- Au coucher : Heure :_____



Note : _____

<u>Interférences avec les activités quotidiennes :</u>

Sur les échelles visuelles ci-dessous, vous devez quantifier une fois par jour seulement l'intensité avec laquelle la chirurgie interfère avec vos activités quotidiennes en prenant soin de noter l'heure correspondante.

- Jour 6: Heure :_____

Est-ce que la chirurgie interfère avec votre capacité à mastiquer les aliments de votre choix ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à ouvrir grand la bouche ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à parler ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à dormir ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à aller au travail ou à l'école ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à mener une vie sociale normale ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à participer à votre activité récréative préférée ?

Pas du tout Extrêmement

JOUR 7

Prises d'analgésiques :

Veuillez noter ci-dessous l'heure à laquelle vous prenez chacun de vos comprimés d'ibuprofène. Veuillez aussi noter si vous avez pris la médication de secours.

Premier comprimé : _____
Deuxième comprimé : _____
Troisième comprimé : _____
Quatrième comprimé : _____
Avez-vous fait usage de la médication de secours ? _____

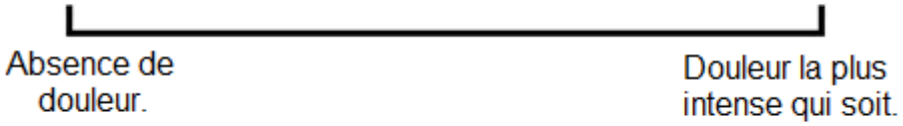
Si oui, à quel moment? Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____
Heure : _____Quantité :_____

Évaluation de la douleur:

Sur les échelles visuelles ci-dessous, vous devez quantifier l'intensité de votre douleur à chaque heure en prenant soin de noter l'heure correspondante jusqu'à l'heure du coucher. Il s'agit dans un premier temps de marquer un trait vertical sur la ligne à l'endroit qui convient selon vous à la douleur que vous ressentez. Vous devez ensuite attribuer à cette même douleur une note qui se situe entre zéro et dix, zéro représentant l'absence de douleur et dix la douleur la plus intense qui soit.

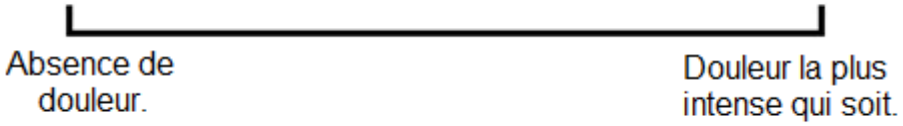
Jour 7.

- Au réveil: Heure :_____



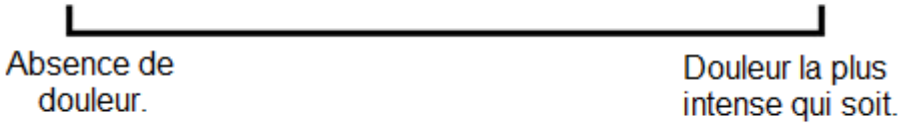
Note : _____

- À midi : Heure :_____



Note : _____

- Au coucher : Heure :_____



Note : _____

Interférences avec les activités quotidiennes :

Sur les échelles visuelles ci-dessous, vous devez quantifier une fois par jour seulement l'intensité avec laquelle la chirurgie interfère avec vos activités quotidiennes en prenant soin de noter l'heure correspondante.

- Jour 7: Heure :_____

Est-ce que la chirurgie interfère avec votre capacité à mastiquer les aliments de votre choix ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à ouvrir grand la bouche ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à parler ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à dormir ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à aller au travail ou à l'école ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à mener une vie sociale normale ?

Pas du tout Extrêmement

Est-ce que la chirurgie interfère avec votre capacité à participer à votre activité récréative préférée ?

Pas du tout Extrêmement

*** N.B. : N'oubliez pas de nous rapporter tous les médicaments que vous n'aurez pas pris afin que nous puissions les collecter.**

APPENDIX VII. CLINICAL AND RADIOGRAPHICAL DATA COLLECTION FORMS

FORMULAIRE DE COLLECTE DE DONNÉES CLINIQUES ET RADIOGRAPHIQUES

Pour projet intitulé « Comparaison de deux différents régimes d'antibiotiques pour la pose d'implant dentaires : une étude clinique randomisée »

No. dossier / Code d'identification :_____

Date de l'intervention: _____

Durée de l'intervention: _____h_____min

Paramètres	Implant no.___	Implant no.___
Longueur de l'incision (mm)		
Système d'implant (compagnie)		
Dimensions d'implant (diamètre par longueur)		
Torque à l'insertion		

(N/cm)		
Qualité osseuse (type I, II, III, IV)		

- Radiographie(s) périapicale(s): Réglages : Appareil:_____

Salle : _____

KV: _____

MA: _____

Durée d'exposition: _____sec

DONNÉES CLINIQUES ET IMMUNOLOGIQUES À UNE SEMAINE POSTOPÉRATOIRE

Date : | | | | / | | | / | | |
a a m m j j

No. de dossier/ Code d'identification : | | | | | | | | | | |

Ne pas oublier de collecter auprès du patient le Questionnaire sur la douleur et l'inconfort ainsi que le Journal de bord. Confirmer avec patient la veille et lui rappeler d'apporter ces deux documents.

Implant no._____:

- Enflure (0 = aucune; 1 = légère; 2 = modérée; 3 = sévère): _____
- Ecchymose (0 = aucune; 1 = présente): _____
- Suppuration (0 = aucune; 1 = présente): _____
- Déhiscence du lambeau (0 = aucune; 1 = présente): _____

- Indice de plaque modifié (PI)

(0 = aucune plaque, 1 = plaque détectée après le passage de la sonde, 2 = plaque peut être observée à l'œil nu, 3 = abondance de plaque) :

Mésial : ____ Buccal :_____ Distal :_____ Lingual : ____

Implant no._____:

- Enflure (0 = aucune; 1 = légère; 2 = modérée; 3 = sévère): _____
- Ecchymose (0 = aucune; 1 = présente): _____
- Suppuration (0 = aucune; 1 = présente): _____
- Déhiscence du lambeau (0 = aucune; 1 = présente): _____

- Indice de plaque modifié (PI)

(0 = aucune plaque, 1 = plaque détectée après le passage de la sonde, 2 = plaque peut être observée à l'œil nu, 3 = abondance de plaque) :

Mésial : ____ Buccal :_____ Distal :_____ Lingual : ____

DONNÉES CLINIQUES ET IMMUNOLOGIQUES À TROIS SEMAINES POSTOPÉRATOIRES

Date : No. de dossier/ Code d'identification :

				/			/				
a	a				m	m		j	j		

Implant no._____:

- Enflure (0 = aucune; 1 = légère; 2 = modérée; 3 = sévère): _____
- Ecchymose (0 = aucune; 1 = présente): _____
- Suppuration (0 = aucune; 1 = présente): _____
- Déhiscence du lambeau (0 = aucune; 1 = présente): _____

- Indice de plaque modifié (PI)

(0 = aucune plaque, 1 = plaque détectée après le passage de la sonde, 2 = plaque peut être observée à l'œil nu, 3 = abondance de plaque) :

Mésial : ____ Buccal :_____ Distal :_____ Lingual : ____

Implant no._____:

- Enflure (0 = aucune; 1 = légère; 2 = modérée; 3 = sévère): _____
- Ecchymose (0 = aucune; 1 = présente): _____

- Suppuration (0 = aucune; 1 = présente): _____

- Déhiscence du lambeau (0 = aucune; 1 = présente): _____

- Indice de plaque modifié (PI)

(0 = aucune plaque, 1 = plaque détectée après le passage de la sonde, 2 = plaque peut être observée à l'œil nu, 3 = abondance de plaque) :

Mésial : ____ Buccal :_____ Distal :_____ Lingual : ____

DONNÉES RADIOGRAPHIQUES, CLINIQUES, ET IMMUNOLOGIQUES À 16 SEMAINES POSTOPÉRATOIRES

Date : / /
a a m m j j

No. de dossier/ Code d'identification :

	Implant no.___	Implant no.___
Signes cliniques d'échec		
Mobilité		
Douleur		
Infection		
Neuropathie (brulure, choc électrique, sensation de froid douloureuse, picotement, démangeaison)		
Paresthésie (perte de sensation)		
Suppuration		
Signes radiographiques d'échec		
Lésion radiolucide		

Légende :

Codes pour les signes cliniques et radiographiques d'échec :

0 = Absence

1 = Présence

Implant no._____:

- Indice de plaque modifié (PI)

(0 = aucune plaque, 1 = plaque détectée après le passage de la sonde, 2 = plaque peut être observée à l'œil nu, 3 = abondance de plaque) :

Mésial : ____ Buccal :_____ Distal :_____ Lingual : ____

Implant no._____:

- Indice de plaque modifié (PI)

(0 = aucune plaque, 1 = plaque détectée après le passage de la sonde, 2 = plaque peut être observée à l'œil nu, 3 = abondance de plaque) :

Mésial : ____ Buccal :_____ Distal :_____ Lingual : ____

Radiographie(s) périapicale(s): Réglages : Appareil:_____

Salle : _____

KV: _____

MA: _____

Durée d'exposition: _____sec

DONNÉES RADIOGRAPHIQUES À 1 AN POSTOPÉRATOIRE

Date : ☐☐☐☐ / ☐☐ / ☐☐

No. de dossier/ Code d'identification : ☐☐☐☐☐☐☐☐☐☐

Radiographie(s) périapicale(s): Réglages : Appareil:_____

Salle : _____

KV: _____

MA: _____

Durée d'exposition: _____sec

APPENDIX VIII. INFORMATION TO RECRUIT PARTICIPANTS

Université de Montréal
Faculté de médecine dentaire

Patients recherchés pour participer au projet de recherche intitulé:
« Comparaison de deux différents régimes d'antibiotiques pour la pose d'implants dentaires : une étude clinique randomisée »

Vous pouvez faire partie de cette étude si:

- Vous avez une gencive relativement en bonne santé et que votre hygiène buccodentaire est bonne.
- Vous êtes partiellement édenté et vous désirez remplacer une ou plusieurs dents manquantes par une couronne ou un pont fixe sur implants.
- Vous présentez un volume osseux et gingival pouvant recevoir la pose d'un implant sans avoir recourt à une greffe osseuse ou gingivale lors de la chirurgie implantaire.
- Vous pouvez donner votre consentement écrit et suivre toutes les procédures de l'étude.

Une compensation de 100 $ vous sera allouée pour votre participation et des analgésiques et antibiotiques à prendre après la chirurgie (valeur approximative de 10 $) vous seront distribués sans frais. Veuillez noter que la fréquence et la durée des étapes cliniques (ex. : rendez-vous de suivi liés à la chirurgie et la restauration de l'implant) seront les mêmes que si vous ne faisiez pas partie de cette étude. Une certaine période de temps (environ 15 minutes) vous sera nécessaire à chaque jour pour remplir les questionnaires liés à ce projet pour la première semaine après la chirurgie.

Pour de plus amples informations, veuillez contactez Dr Robert Durand au 514 343-7464.

L'équipe de recherche liée à ce projet comprend les membres suivants :

- Dr Robert Durand, chercheur principal et chirurgien;
- Dr Issam Kersheh, assistant de recherche
- Dre Nathalie Rei, co-chercheur et spécialiste en médecine buccale;
- Dr René Voyer, co-chercheur et chirurgien;
- Dr Pierre Boudrias, co-chercheur et chirurgien;
- M. Pierre Rompré, statisticien.