AUTHOR QUERY FORM

ELSEVIER	**Journal:** JJOD **Article Number:** 2264	**Please e-mail or fax your responses and any corrections to:** **E-mail:** corrections.eseo@elsevier.thomsondigital.com **Fax:** +353 6170 9272

Dear Author,

Please check your proof carefully and mark all corrections at the appropriate place in the proof (e.g., by using on-screen annotation in the PDF file) or compile them in a separate list. Note: if you opt to annotate the file with software other than Adobe Reader then please also highlight the appropriate place in the PDF file. To ensure fast publication of your paper please return your corrections within 48 hours.

For correction or revision of any artwork, please consult http://www.elsevier.com/artworkinstructions.

Any queries or remarks that have arisen during the processing of your manuscript are listed below and highlighted by flags in the proof. Click on the 'Q' link to go to the location in the proof.

Location in article	Query / Remark: click on the Q link to go Please insert your reply or correction at the corresponding line in the proof
Q1	Please confirm that given names and surnames have been identified correctly.

Please check this box or indicate your approval if you have no corrections to make to the PDF file ☐

Thank you for your assistance.

Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.intl.elsevierhealth.com/journals/jden

Outcome of single immediate implants placed in post-extraction infected and non-infected sites, restored with cemented crowns: A 3-year prospective study

Carlos Torres-Sánchez[a], Raquel Castillo-Oyagüe[b,*], Vanesa Montoya-Salazar[a], Christopher D. Lynch[c], José-Luis Gutiérrez-Pérez[a], Daniel Torres-Lagares[a]

[a] Department of Stomatology, Faculty of Dentistry, University of Seville (US), C/Avicena s/n, 41009 Sevilla, Spain
[b] Department of Buccofacial Prostheses, Faculty of Dentistry, Complutense University of Madrid (UCM), Pza. Ramón y Cajal s/n, 28040 Madrid, Spain
[c] School of Dentistry, Cardiff University, CF14 4XY Cardiff, Wales, UK

ARTICLE INFO

Article history:
Received 27 December 2013
Received in revised form
14 March 2014
Accepted 17 March 2014
Available online xxx

Keywords:
Fresh-socket
Periapical lesion
Postextraction infected alveoli
Postextraction non-infected site
Immediate implant placement

ABSTRACT

Objectives: To compare the survival of immediate implants placed in postextraction infected and non-infected sites, restored with cemented crowns.
Methods: Thirty-six implants were immediately placed in non-infected sockets (control group (CG), $n = 18$), and in infected alveoli (test group (TG), $n = 18$) that had been debrided, curetted, cleaned with 90% hydrogen peroxide, irradiated with yttrium–scandium–gallium–garnet (Er,Cr:YSGG) laser, and irrigated with a sterile solution. Guided bone regeneration was performed under antibiotic coverture. All study patients had both a CG and a TG site. The implant osteotomy sites were extended 3–4 mm beyond the apical extent of the sockets to achieve primary stability for the implants. The prosthetic phase occurred 4.5 months after surgery. Success criteria were accepted as the presence of implant stability, absence of a radiolucent zone around the implants, absence of mucosal suppuration, and lack of pain. Clinical evaluations were performed at baseline, and at 12, 24, and 36 months of follow-up.
Results: All of the implants were osseointegrated 3 months after surgery. The 3-year survival rate was 94.44% for TG, and 100% for CG. The clinical and radiographic variables tested yielded no significant differences among groups at 36 months.
Conclusions: Under the tested conditions, immediate implant placement can be considered a predictable treatment option for the restoration of fresh postextraction infected sockets.
Clinical significance: Immediate implants may be indicated for replacing teeth lost due to chronic periapical lesions with endodontic failure history when appropriate preoperative procedures are taken to clean and decontaminate the surgical sites.

© 2014 Published by Elsevier Ltd.

* *Corresponding author at:* Department of Buccofacial Prostheses, Faculty of Dentistry, Complutense University of Madrid (UCM), Pza. Ramón y Cajal s/n, E-28040 Madrid, Spain. Tel.: +34 607367903; fax: +34 913942029.
E-mail addresses: raquel.castillo@odon.ucm.es, siete_rosas.rc@hotmail.com (R. Castillo-Oyagüe).

http://dx.doi.org/10.1016/j.jdent.2014.03.008
0300-5712/© 2014 Published by Elsevier Ltd.

UNCORRECTED PROOF

Please cite this article in press as: Torres-Sánchez DTDDIFFDC, et al. Outcome of single immediate implants placed in post-extraction infected and non-infected sites, restored with cemented crowns: A 3-year prospective study. Journal of Dentistry (2014), http://dx.doi.org/10.1016/j.jdent.2014.03.008

1. Introduction

To date, only few studies have reported on the clinical outcomes of immediate implants inserted in postextraction sockets.[1] The technique of immediate implant placement was first described by Lazzara[2] in 1989. This one-step surgical procedure reduces treatment time, improves aesthetic outcomes, increases comfort during healing, and has proven to be a predictable strategy with a high success rate[3,4] in absence of periapical lesions.[5–9] In contrast with the traditional protocol, the immediate placement of an implant after tooth extraction also maintains the horizontal and vertical dimensions of the osseous tissues, and keeps the implants at the same angulation as the pre-existing natural teeth.[10]

Furthermore, using implants to replace endodontically compromised teeth has been proposed when periapical surgery is inadvisable.[10,11] Even though some local and systemic factors could contraindicate dental implant placement,[11] recent investigations verify that the presence of a periradicular infection may not be an inconvenience for immediate implants[12,13] if the surgical sites are appropriately cleaned and decontaminated.[4,14] In these cases, guided bone regeneration (GBR) is usually performed to fill the bone-implant gap and/or other bone deficiencies. Although controversial, systemic antibiotics have also been recommended until further controlled trials prove otherwise.[15] However, there is insufficient evidence about what cleaning protocol would be the most suitable prior to placing implants in postextraction infected sites,[16–18] even when much of the information available comes from randomized controlled trials.[19]

Therefore, the aim of this study was to assess the outcome of immediate implants used to replace teeth with chronic periapical lesions after treating the infected sockets in the hope of controlling the infection. The success of these implants was compared with immediate implants placed in non-infected sockets within the same patients. Notwithstanding the cleaning and surgical protocol proposed (which combines different procedures reported separately in the literature), the major novelty of this 3-year prospective study is that each patient included both infected and non-infected sites (controls).

The null hypothesis tested stated that there is no difference in the maintenance and health of the peri-implant soft and hard tissues over time among implants inserted after the extraction of periapically affected and non-affected teeth, under controlled conditions.

2. Materials and methods

Thirty-six human teeth including incisors ($n = 10$), canines ($n = 10$), and premolars ($n = 16$) were extracted, and 36 titanium implants (MIS Ibérica, C1, Shlomi, Israel) were immediately placed after extraction. Half of the implants were inserted in non-infected sites (control group (CG), $n = 18$) and the remaining half were immediately placed in infected sites after being debrided, curetted, cleaned with 90% hydrogen peroxide, and irradiated with yttrium–scandium–gallium–garnet (Er,Cr:YSGG) laser (test group (TG), $n = 18$). All of the study patients had both CG and TG sites that required extraction, simultaneously (Fig. 1). The teeth were matched in all cases (*e.g.*, canine in CG and TG for same patient, *etc.*).

The inclusion criteria were: partially edentulous patients aged between 18 and 50 years, with 26 or more teeth, needing the extraction of 2 maxillary teeth (being incisors, canines, or premolars), having a chronic periapical lesion of endodontic or endoperiodontal origin in one of these sites as determined by clinical and radiographic evaluation, with no medical contraindications for oral surgical procedures (American Society of Anesthesiologists Class 1 or 2) (http://www.asahq.org/), full-mouth plaque scores and full-mouth bleeding scores of less than 25% at baseline, presence of adequate quality and quantity of native bone to achieve primary stability, and presence of sufficient mesiodistal space for immediate implant placement (>7 mm).

The study included several exclusion criteria. Patients were excluded based on any disease, condition, or medication that might compromise the healing or the osseointegration: presence of apical lesions that exceeded twice the diameter of the middle third of the root; complete loss of the vestibular or palatal/lingual alveolar wall; inability or refusal to return for follow-up visits; and inability or unwillingness to maintain a good level of oral hygiene during the study period.

The clinical trial was conducted following the ethical principles of medical investigation involving human subjects under the Helsinki Declaration of the World Medical Association (http://www.wma.net) and the Spanish Law 14/2007 of July 3rd for Biomedical Research (http://www.boe.es). All of the participants were given a detailed explanation about the

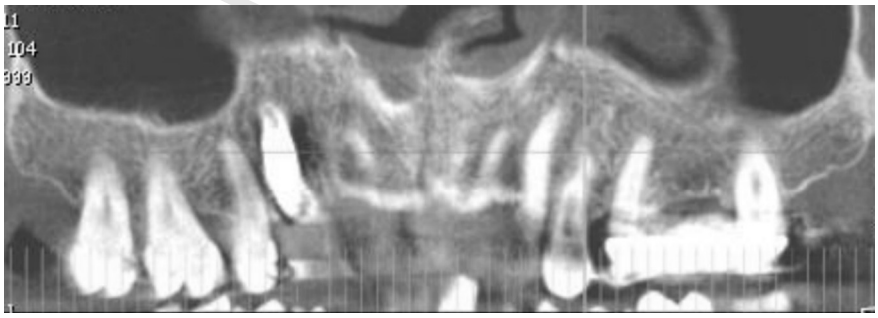

Fig. 1 – Computed tomography (CT) of a study patient showing 'tooth 14' with a periapical lesion and 'tooth 24' without signs of periapical infection.

Please cite this article in press as: Torres-Sánchez DTDDIFFDC, et al. Outcome of single immediate implants placed in post-extraction infected and non-infected sites, restored with cemented crowns: A 3-year prospective study. Journal of Dentistry (2014), http://dx.doi.org/10.1016/j.jdent.2014.03.008

UNCORRECTED PROOF

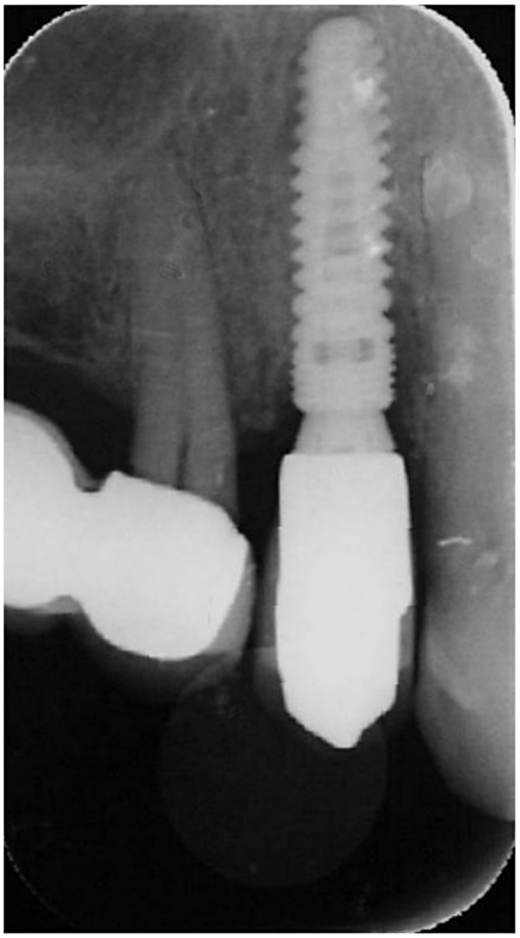

Fig. 2 – Implant placed in a non-infected alveolus ('tooth 24') at 12 months of follow-up (CG).

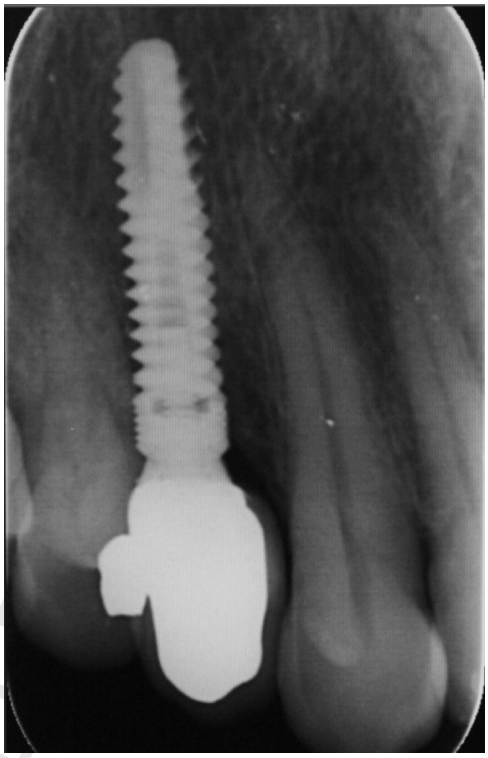

Fig. 3 – Implant placed in a post-extraction infected site ('tooth 14') at 36 months of follow-up (TG).

purpose and process of the study. The Ethics Committee Approval (Court of Ethics at the University of Seville, US, Spain) and the patients' approved written consent were obtained.

Successful osseointegration of the immediate implants was determined at 12, 24, and 36 months of follow-up for CG (Fig. 2) and TG (Fig. 3).

2.1. *Clinical procedure*

The teeth of the CG, which were periodontally compromised, were treated one month before surgery with scaling and root planning. Subsequently, all patients underwent antibiotic treatment with Azithromycin in a single dose of 250 mg/day for 5 days after an initial loading dose of 500 mg,[20] to stop any active periodontal infection.

One month later, patients were prescribed 1.5 g of amoxicillin (or 0.9 g of clindamycin in penicillin-sensitive patients). The total daily dosage of antibiotic was administered in 3 equal doses every 8 h. The antibiotic treatment started 4 days before surgery and was kept for a total of 10 days.[21] All procedures were carried out under local anaesthesia. A full-thickness mucoperiosteal flap was reflected at the surgical site, and the affected teeth were extracted with minimal trauma to the cortical plates.

Only in case of the TG sites, the extraction sockets were meticulously curetted and debrided to remove all the detected granulation and infected tissues. Such sockets were then cleaned with 90% hydrogen peroxide and laser-irradiated with special attention to the periapical area. A Waterlase MD erbium, chromium: yttrium–scandium–gallium–garnet (Er,Cr:YSGG) laser (Biolase Technology, Irvine, CA, USA) emitting at 2780-nm wavelength was utilized. A MZ-4 tip was inserted into each TG alveolus and then fired at a power setting of 0.5 W (7 water/14 air) and a repetition rate of 20 Hz in a clockwise fashion, describing a coronary movement with an oscillatory technique. The laser power emitted at the fibre tip was measured by a wattmeter (Field Master, Coherent Inc., Auburn, CA, USA) before each irradiation to ensure stable and standardized power outputs.[22] Approximately 60 s were spent to detoxify the alveoli, focusing on the area that showed the greatest concentration of infection.[23] The procedure was concluded with vigorous irrigations of the surgical sites using a sterile saline solution.

2.2. *Surgical area*

The surgical area was prepared following the standard protocol for implant placement, and the site preparation was extended apically 3–4 mm to achieve primary stability for the implants. Moderate modifications of the sockets were accomplished at this stage to establish a better position and angulation of the implants; however, further aggravation of the already-existing bone deficiency was avoided. Thereafter,

UNCORRECTED

Please cite this article in press as: Torres-Sánchez DTDDIFFDC, et al. Outcome of single immediate implants placed in post-extraction infected and non-infected sites, restored with cemented crowns: A 3-year prospective study. Journal of Dentistry (2014), http://dx.doi.org/10.1016/j.jdent.2014.03.008

the endosseous titanium dental implants (C1 implants, standard platform: Ø 4.20 mm × 13 mm, Mis Ibérica, Barcelona, Spain) were immediately introduced into the prepared sites and evaluated for primary stability. The residual alveolar defect was filled with bovine-derived bone mineral (Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) to achieve complete coverage of the immediate implants, and a titanium-reinforced expanded tetrafluoroethylene membrane (Gore-Tex, WL Gore & Associates Inc., Flagstaff, AZ, USA) was secured over the site to commence the guided bone regeneration. The surgical procedure was concluded by suturing the flap (Gore-Tex sutures, WL Gore & Associates Inc.) to achieve soft tissue primary closure. The healing period was monitored to ensure sustained closure of the site and infection-free regeneration. All of the implants were placed by specialists (oral surgeons) with at least 5 years of experience.

With regard to the postoperative management, patients were prescribed twice-daily rinses with 10 ml of 0.12% chlorhexidine solution for 14 days, and were cited weekly for a month. Two weeks after the surgery, an acrylic-based provisional removable dental prosthesis (RDP) with wrought-wire clasps was made to replace the extracted teeth. The second-stage surgical procedure was performed 3 months after the first-stage operation.

2.3. Crown restorations

The second-stage surgery was carried out 3 months after implant placement. In both study groups, appropriate transfer copings (CS I0375, Mis Ibérica) were connected to the implants. A single-phase silicone impression technique with individual trays was selected (Imprint II, 3M ESPE, Flexitime, Heraeus-Kulzer, Wehrheim, Germany). Prefabricated titanium abutments (CS CPK61 standard platform: Ø 4.20 mm, Mis Ibérica) were screwed onto the osseointegrated implants with a torque of 35 N cm. Customized acrylic crowns were luted using an acrylic/urethane-based material (Temp-bond NE, Orange, CA, USA). The axial surfaces of the abutments were varnished with a thin layer of cement before inserting each structure to counteract the thyrotrophic behaviour of the luting agent.

Six weeks later, the provisional crowns were replaced by Co–Cr-based metal-ceramic prostheses. The crown copings were vacuum-cast in a base metal alloy of white Co–Cr for ceramics (Heraenium CoCr metal ceramic alloy, Heraeus-Kulzer, Wehrheim, Germany). Wax-patterns were invested with a commercial phosphate-bonded stone (IPS Press Vest Speed, Ivoclar-Vivadent AG, Schaän, Liechtenstein) by using cylinders without a metal ring. The vacuum casting of the Co–Cr specimens was carried out in an induction centrifugal machine (MIE-200 C/R, Ordenta, Arganda del Rey, Madrid, Spain) under vacuum pressure (580 mm Hg) at 1465 °C.[24–27] Oxidation of the crown frameworks was completed in a ceramic oven (Programat P500/G2, Ivoclar-Vivadent AG, Schaän, Liechtenstein). Two layers of opaque porcelain were applied that underwent two separate firing cycles of 30 min/cycle in the same oven. The first layer was heated at 950 °C.[26,28] The structures were then coated by the stratification technique with dentine and enamel feldespathic ceramic (HeraCeram, Heraeus Kulzer, Wehrheim, Germany) at 850 °C in every cycle. The glaze firing was performed at 810 °C.[26] The definitive crowns were luted with glass-ionomer cement (Ketac Cem, 3M Espe, Seefeld, Germany).

2.4. Implant success criteria

Implant success criteria included: no clinically detectable implant mobility at the second-stage surgery or at the follow-up evaluations, no radiographic evidence of peri-implant radiolucency, no signs or symptoms of infection, and no bone loss in excess (<2 mm), considering the criteria reported by Albrektsson et al.[29]

2.5. Follow-up

The next clinical parameters were checked: pain, occlusion, prosthesis mobility and fulfilment of the success criteria. Follow-up examinations were performed at baseline and at 12, 24, and 36 months (Figs. 2 and 3). The probing depth (PD), modified plaque index (mPI), and modified bleeding index (mBI)[30] were measured on the mesial, distal, buccal, and palatal surfaces of the implants using a periodontal probe (Hu-Friedy PGF-GFS, Hu-Friedy, Chicago, IL, USA). The distance between the platform of the implant and the marginal gingival level (MGL) was measured at 4 sites per implant at the same surfaces as for the mPI. The width of the keratinized mucosa (KM) was recorded at the mid-buccal position.

Intraoral digital radiographs (Schick CDR, Schick Technologies, Long Island City, NY, USA) were also obtained at baseline and at 12, 24, and 36 months after implant placement. Periapical radiographs were taken perpendicularly to the long axis of the implants following a long-cone parallel technique with an occlusal template to measure the marginal bone level and to calibrate the changes in marginal bone height over time. The marginal bone level was considered from the reference point represented by the more coronal portion of the implant in contact with the bone to the point where the bone tissue met the implant surface at the mesial and distal sites. The differences in bone level were measured using specific software (Schick CDR, Schick Technologies).

2.6. Statistical analysis

The statistical analysis included descriptive statistics for all parameters tested. Clinical data and radiographic bone levels (mesial, distal, and mean bone loss in millimetres) were reported for each implant and study group by both a measure of centrality (mean) and a measure of variability (standard deviation: SD) at baseline and at 12, 24, and 36 months.[5,13,31,32]

The normal distribution of the data was proved with the Kolmogorov–Smirnov test.[32] Taking into account that the risk of implant failure significantly differs across subjects, the assumption of independence of implants within the same subject was not valid. Therefore, to evaluate the differences among TG and CG at every time point, a two-tailed Student's t test was run for each clinic/radiographic variable.[32]

Between-group comparisons of the survival rates were made with the χ^2 and the Fisher's exact test at 12, 24, and 36 months of follow-up.[33]

The statistical analyses were selected according to the requirements for the design of clinical trials in implant

UNCORRECTED PROOF

Table 1 – Clinical parameters measured at baseline, 12, 24, and 36 months of follow-up (n = 36 implants).

Parameter	CG				TG			
	Baseline	12 months	24 months	36 months	Baseline	12 months	24 months	36 months
PD	2.39 ± 0.40	2.44 ± 0.28	2.60 ± 0.37	2.53 ± 0.44	2.46 ± 0.44	2.53 ± 0.44	2.76 ± 0.80	2.51 ± 0.44
PD DIF BASELINE		−0.05 ± 0.37	−0.21 ± 0.50	−0.13 ± 0.43		−0.06 ± 0.38	−0.30 ± 0.74	−0.05 ± 0.53
mPI	0.94 ± 1.10	1.66 ± 0.84(*)	1.16 ± 1.04	1.00 ± 1.02	1.11 ± 0.67	0.83 ± 0.85(*)	1.27 ± 0.82	0.88 ± 0.83
mPI DIF BASELINE		−0.72 ± 0.89(**)	−0.22 ± 0.94	−0.05 ± 0.72		0.27 ± 0.89(**)	−0.16 ± 1.09	0.22 ± 0.87
mBI	0.66 ± 0.76	1.38 ± 0.84(***)	1.05 ± 0.99	1.00 ± 1.02	0.88 ± 0.58	0.88 ± 0.75(***)	0.83 ± 0.85	0.94 ± 0.63
mBI DIF BASELINE		−0.72 ± 0.75(****)	−0.38 ± 0.77	−0.33 ± 0.84		0.0 ± 0.68(****)	0.05 ± 0.87	−0.05 ± 0.80
MGL	1.16 ± 0.29	1.13 ± 0.23	1.11 ± 0.21	1.16 ± 0.24	0.88 ± 0.58	0.88 ± 0.75	0.83 ± 0.85	1.00 ± 0.59
MGL DIF BASELINE		0.02 ± 0.31	0.05 ± 0.23	0.00 ± 0.29		0.00 ± 0.68	0.05 ± 0.87	−0.11 ± 0.67
KM	2.61 ± 0.69(*****)	2.74 ± 0.73(******)	2.61 ± 1.14	2.88 ± 1.27	3.55 ± 0.92(*****)	3.33 ± 1.08(******)	3.33 ± 1.08	3.38 ± 0.60
KM DIF BASELINE		0.13 ± 0.47	0.00 ± 0.76	−0.27 ± 0.82		0.22 ± 0.42	0.22 ± 0.42	0.16 ± 0.98

CG: Control group. TG: Test group. Units: mm.
PD (probing depth), PD DIF BASELINE (difference to baseline in probing depth), mPI (modified plaque index), mPI DIF BASELINE (difference to baseline in modified plaque index), mBI (modified bleeding index), mBI DIF BASELINE (difference to baseline in modified bleeding index), MGL (marginal gingival level), MGL DIF BASELINE (difference to baseline in marginal gingival level), KM (width of the keratinized mucosa), KM DIF BASELINE (difference to baseline in width of the keratinized mucosa).
Significant differences are marked by pairs of equal asterisks (*,*) (**,**) (***,***) (****,****) (*****,*****) (******,******).

dentistry revised at the 8th European Workshop on Periodontology[34] as well as the recommendations of Hannigan and Lynch for oral and dental research.[32] Data were processed using the Statistical Package for the Social Sciences (software v.20) (SPSS/PC+, Inc.; Chicago, IL, USA) taking the cut-off level for statistical significance at $\alpha = 0.05$.[12,14,32]

3. Results

The study findings are reported in Tables 1 and 2. The survival rates of TG and CG were not significantly different ($p = 0.720$). TG registered a survival rate of 100% at 12 and 24 months (18/18), and of 94.44% at 36 months (17/18). The failure for the single lost implant in the TG at 36 months was attributed to the poor hygiene and insufficient collaboration of the patient.

CG observed a survival rate of 100% at the three time points evaluated (18/18).

3.1. *Clinical parameters*

Data obtained for clinical factors are reported in Table 1. Neither group yielded significant changes in PD from baseline to 36 months of follow-up ($p = 0.739$–0.132). At 36 months of follow-up, mean (±SD) PD values were 2.51 ± 0.44 mm for TG, and 2.53 ± 0.44 mm for CG, showing no significant differences ($p = 0.739$).

The mean (±SD) mPI scores were statistically similar at baseline, 24, and 36 months of follow-up; being 0.88 ± 0.83 mm for TG, and 1.00 ± 1.02 mm for CG at 3-year evaluation ($p = 0.724$). Significant changes in mPI were only detected at 12 months of follow-up, so that lower values were recorded for TG than for CG ($p = 0.049$).

The mean (±SD) mBI measures were statistically comparable at baseline, 24, and 36 months of follow-up; being 0.94 ± 0.63 mm for TG, and 1.00 ± 1.02 mm for CG at 3-year evaluation ($p = 0.847$). Significant changes in mBI only occurred at 12 months of follow-up, so that TG achieved the lowest values ($p = 0.045$).

Neither significant differences at any time point nor changes at follow-up were registered for the MGL variable ($p = 0.278$–0.081). The mean (±SD) MGL scores at 36 months were 1.00 ± 0.59 mm for TG, and 1.16 ± 0.24 mm for CG.

Significant differences in KM were observed at baseline between both groups, being higher for TG ($p = 0.032$). Such discrepancy was maintained at 12 months of follow-up ($p = 0.045$). Neither group showed significant changes in KM between baseline and 1-year evaluation ($p > 0.05$) (Table 1).

Table 2 – Radiographic results: marginal bone level at baseline, 12, 24, and 36 months after implant placement (n = 36 implants).

	Bone loss (mm)					
	CG			TG		
	Mesial	Distal	Mean (SD)	Mesial	Distal	Mean (SD)
Baseline	1.05 ± 0.22(*)	1.27 ± 0.51	1.16 ± 0.27	1.36 ± 0.46(*)	1.36 ± 0.37	1.36 ± 0.39
12 months	0.82 ± 0.47	0.65 ± 0.23	0.73 ± 0.29	0.77 ± 0.22	0.70 ± 0.35	0.73 ± 0.22
24 months	0.52 ± 0.19	0.56 ± 0.16(**)	0.54 ± 0.15(***)	1.48 ± 2.63	0.81 ± 0.17(**)	0.84 ± 0.15(***)
36 months	0.60 ± 0.22(****)	0.60 ± 0.20	0.60 ± 0.16	0.47 ± 0.11(****)	0.60 ± 0.19	0.53 ± 0.13

CG: Control group. TG: Test group. Units: mm.
Significant differences are marked by pairs of equal asterisks (*,*) (**,**) (***,***) (****,****).

Please cite this article in press as: Torres-Sánchez DTDDIFFDC, et al. Outcome of single immediate implants placed in post-extraction infected and non-infected sites, restored with cemented crowns: A 3-year prospective study. Journal of Dentistry (2014), http://dx.doi.org/10.1016/j.jdent.2014.03.008

The mean (±SD) KM results at 36 months were statistically comparable (3.38 ± 0.60 mm for TG, and 2.88 ± 1.27 mm for CG; $p = 0.150$).

3.2. *Radiographic assessment*

Radiographic results are reported in Table 2. At baseline, the marginal mesial bone level of TG was significantly higher than that of CG (1.36 ± 0.46 mm *vs.* 1.05 ± 0.22 mm) ($p = 0.015$).

At 12 months, no significant differences in marginal bone height were registered among groups ($p > 0.05$).

At 24 months, TG exhibited significantly lower marginal distal bone loss (0.81 ± 0.17 mm *vs.* 0.56 ± 0.16 mm) and mean marginal bone loss (0.84 ± 0.15 mm *vs.* 0.54 ± 0.15 mm) than did CG ($p = 0.0001$ in both cases).

At 36-month follow-up, both groups showed comparable maintenance of marginal bone levels resulting in an average marginal bone height of 0.53 ± 0.13 mm for TG, and 0.60 ± 0.16 mm for CG ($p = 0.213$). At 3-year evaluation, only the marginal mesial bone level showed significant differences among groups, being lower for TG than for CG ($p = 0.032$).

4. Discussion

The concept of immediate placement of dental implants after removing a tooth with periapical pathology is still a matter of debate.[12,15,31,35] Even though this technique minimizes the number of surgical procedures by combining extraction, implant insertion, and bone grafting in one appointment, there is a potential risk for contamination during the initial healing period due to remnants of infection.[12]

This prospective clinical trial evaluated immediate implants placed in the anterior maxilla. The protocol was rigorously standardized so that each participant had one periapically and one non-periapically affected maxillary tooth (being incisors, canines, or premolars in both CG and TG sites) indicated for extraction (Fig. 1). Hence, the sample size was a bit lower than that used in related investigations.[1,36,37] While previous research included two separated groups of volunteers depending on the presence or absence of periapical disease in the teeth extracted,[31,37] our method attempts to reach more accurate results limiting the inter-subject variability.[38]

This study shows comparable success rates to those reported in the literature[7,14,31,37,39] when the implants were positioned in presence of chronic apical lesions under controlled conditions.[13,31] The null hypothesis was accepted, since the maintenance and health of the peri-implant soft and hard tissues over time was similar and favourable in TG and CG (Tables 1 and 2; Figs. 2 and 3). In this regard, mPI and mBI values did not register any significant differences between groups at baseline, 24, and 36 months of follow-up. KM results were statistically comparable among TG and CG at 2-year and 3-year evaluation. Moreover, PD, and MGL scores were statistically similar at any time point evaluated regardless of the presence or absence of periapical infection in the teeth replaced by the implants ($p > 0.05$) (Table 1). Finally, the average marginal bone level at baseline, 1-year, and 3-year evaluation did not depend on the existence of periapical disease in the teeth extracted (Table 2). Clinical trials of longer duration are required to corroborate these promising findings.

In an animal experiment in which immediate implants were placed in presence of periapical infection,[14] the histomorphometric analysis revealed no significant differences in the percentage of bone-to-implant contact (BIC) between the periapically infected and the healthy sites at 12 weeks of follow-up. A former animal study showed the same trend.[2] However, clinical trials developed in humans have traditionally suggested that history of periodontal or endodontic infections may be a predictive marker for implant infection and failure.[21,33] This fact has led most clinicians to avoid the immediate placement of endosseous dental implants at infected sites, and to consider infection as a possible contraindication for immediate implantation.[21] Nonetheless, our results suggest that immediate implants may be successfully introduced into debrided infected dentoalveolar sockets under a controlled procedure, which is in agreement with other authors.[21,33] According to Crespi *et al*,[31] the high success rates of immediate implants placed in sockets with chronic diseases may be explained through the endoperiodontal origin of the infection, which is associated with anaerobic bacteria commonly restricted in the infected root canal (Fusobacterium, Prevotella, Porphyromonas, Actinomyces, Streptococcus, Peptostreptococcus).[31,40,41] The subsequent variations in the anaerobic environment that occur after the extraction and curettage of the socket would lead to the eradication of the associated endoperiodontal microbiota.[31]

After the debridement of non-viable tissues, the extraction sockets were cleaned with 90% hydrogen peroxide, irradiated with yttrium–scandium–gallium–garnet (Er,Cr:YSGG) laser, and irrigated with a sterile saline solution in the present study.[37] A (Er,Cr:YSGG) laser with 2780-nm wavelength was chosen because of its ability to ablate infected tissues with minimal thermal side effects, and minimal if any damage of the surrounding tissues.[42] The great decontamination capacity of this laser allows reaching a 98% reduction of pathogenic bacteria, which diminishes the wound healing time and the possibilities for post-operative infections.[18,22,43] It has also been reported that atraumatic extraction of the affected teeth in conjunction with GBR techniques can significantly improve the prognosis of immediate implants placed in either infected or non-infected sites.[21,39,44] In addition, chlorhexidine rinses had been recommended in similar cases.[17] The surgical and cleaning protocol developed (based on the combination of several procedures described separately in the literature), is original in our study and may have contributed to the achievement of positive outcomes in the present trial.

Moreover, the prescription of pre- and postoperative antibiotics may have established a favourable basis for bone healing and osseointegration.[15,17,21] The antibiotic regimen administered in this research was previously reported by Casap et al.[21] Both Lindeboom et al.[12] and Siegenthaler et al.[13] ordered antibiotic prophylaxis (clindamycin 600 mg, 1 h before surgery), while authors such as Novaes and Novaes Jr.,[45] Villa and Rangert[46] and Siegenthaler et al.[13] recommended the use of postoperative antibiotics in different dosages, for different time periods. Thus, there is still no agreement on whether antibiotic therapy should be utilized or not prior to implant placement in presence of periapical infection.

UNCORRECTED PROOF

Please cite this article in press as: Torres-Sánchez DTDDIFFDC, et al. Outcome of single immediate implants placed in post-extraction infected and non-infected sites, restored with cemented crowns: A 3-year prospective study. Journal of Dentistry (2014), http://dx.doi.org/10.1016/j.jdent.2014.03.008

Our study findings reveal that successful immediate implantation in debrided infected sockets mainly depends on the combination of complete removal of all contaminated tissues, controlled regeneration of the alveolar defect, antibiotic coverture, and chlorhexidine rinses.[31,47] This protocol has permitted obtaining a correct osseointegration between titanium structures and bone, regardless of the existence of previous infectious processes.[48]

It would seem prudent for this theme of teaching to further increase in order to best prepare graduating students for independent clinical practice.[49] However, this technique should be limited to experienced surgeons who are highly skilled in differentiating and debriding granulation tissues. Further clinical and histological studies may allow a better understanding of the healing pattern in case of immediate implants placed in debrided infected sites. Our results are positive but should be extrapolated with caution and validated in future investigations developed in other, broader settings in which different positions of the dental arch should be assessed. Also, the oral-health related quality of life (OHRQoL) associated with immediate implant placement may be evaluated using specific questionnaires for implant restorations (such as the QoLIP-10), at different time points[50,51].

5. Conclusions

Within the limitations of this study, two main conclusions may be drawn:

1. Immediate implant placement can be considered as a safe, effective, and predictable treatment option for the restoration of fresh postextraction infected sockets when appropriate preoperative procedures are taken to clean and decontaminate the surgical sites.
2. The combination of debridation, curettage, cleaning with 90% hydrogen peroxide, irradiations with yttrium–scandium–gallium–garnet (Er,Cr:YSGG) laser, and chlorhexidine rinses together with guided bone regeneration under antibiotic coverture may guarantee the durability of immediate implants inserted in infected alveoli.

REFERENCES

1. Mozzati M, Arata V, Gallesio G, Mussano F, Carossa S. Immediate postextraction implant placement with immediate loading for maxillary full-arch rehabilitation: a two-year retrospective analysis. *Journal of the American Dental Association* 2012;**143**:124–33.
2. Lazzara RJ. Immediate implant placement into extraction sites: surgical and restorative advantages. *International Journal of Periodontics and Restorative Dentistry* 1989;**9**:332–43.
3. Covani U, Marconcini S, Galassini G, Cornelini R, Santini S, Barone A. Connective tissue graft used as a biologic barrier to cover an immediate implant. *Journal of Periodontology* 2007;**78**:1644–9.
4. Marconcini S, Barone A, Gelpi F, Briguglio F, Covani U. Immediate implant placement in infected sites: a case series. *Journal of Periodontology* 2013;**84**:196–202.
5. Gelb DA. Immediate implant surgery: three-year retrospective evaluation of 50 consecutive cases. *International Journal of Oral and Maxillofacial Implants* 1993;**8**:388–99.
6. Becker W, Dahlin C, Becker BE, Lekholm U, van Steenberghe D, Higuchi K, *et al*. The use of e-PTFE barrier membranes for bone promotion around titanium implants placed into extraction sockets: a prospective multicenter study. *International Journal of Oral and Maxillofacial Implants* 1994;**9**:31–40.
7. Becker W, Dahlin C, Lekholm U, Bergstrom C, van Steenberghe D, Higuchi K, *et al*. Five-year evaluation of implants placed at extraction and with dehiscences and fenestration defects augmented with ePTFE membranes: results from a prospective multicenter study. *Clinical Implant Dentistry and Related Research* 1999;**1**:27–32.
8. Grunder U, Polizzi G, Goené R, Hatano N, Henry P, Jackson WJ, *et al*. A 3-year prospective multicenter follow-up report on the immediate and delayed-immediate placement of implants. *International Journal of Oral and Maxillofacial Implants* 1999;**14**:210–6.
9. Rosenquist B, Ahmed M. The immediate replacement of teeth by dental implants using homologous bone membranes to seal the sockets: clinical and radiographic findings. *Clinical Oral Implants Research* 2000;**11**:572–82.
10. Chang SW, Shin SY, Hong JR, Yang SM, Yoo HM, Park DS, *et al*. Immediate implant placement into infected and noninfected extraction sockets: a pilot study. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics* 2009;**107**:197–203.
11. Diz P, Scully C, Sanz M. Dental implants in the medically compromised patient. *Journal of Dentistry* 2013;**41**:195–206.
12. Lindeboom JA, Tjiook Y, Kroon FH. Immediate placement of implants in periapical infected sites: a prospective randomized study in 50 patients. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics* 2006;**101**:705–10.
13. Siegenthaler DW, Jung RE, Holderegger C, Roos M, Hämmerle CH. Replacement of teeth exhibiting periapical pathology by immediate implants: a prospective, controlled clinical trial. *Clinical Oral Implants Research* 2007;**18**:727–37.
14. Novaes Jr AB, Vidigal Júnior GM, Novaes AB, Grisi MF, Polloni S, Rosa A. Immediate implants placed into infected sites: a histomorphometric study in dogs. *International Journal of Oral and Maxillofacial Implants* 1998;**13**:422–7.
15. Waasdorp JA, Evian CI, Mandracchia M. Immediate placement of implants into infected sites: a systematic review of the literature. *Journal of Periodontology* 2010;**81**:801–8.
16. Esposito M, Grusovin MG, Polyzos IP, Felice P, Worthington HV. Timing of implant placement after tooth extraction: immediate, immediate-delayed or delayed implants? A Cochrane systematic review. *European Journal of Oral Implantology* 2010;**3**:189–205.
17. Chrcanovic BR, Martins MD, Wennerberg A. Immediate placement of implants into infected sites: a systematic review. *Clinical Implant Dentistry and Related Research* 2013. http://dx.doi.org/10.1111/cid.12098. [in press].
18. Romanos GE, Gupta B, Yunker M, Romanos EB, Malmstrom H. Lasers use in dental implantology. *Implant Dentistry* 2013;**22**:282–8.
19. Thomason JM, Kelly SA, Bendkowski A, Ellis JS. Two implant retained overdentures—a review of the literature supporting the McGill and York consensus statements. *Journal of Dentistry* 2012;**40**:22–34.
20. Abinaya-Prakasam S, Sugumari E, Kumar-Natarajan R. Antibiotics in the management of aggressive periodontitis. *Journal of Pharmacy and Bioallied Sciences* 2012;**4**:S252–5.

UNCORRECTED PROOF

Please cite this article in press as: Torres-Sánchez DTDDIFFDC, et al. Outcome of single immediate implants placed in post-extraction infected and non-infected sites, restored with cemented crowns: A 3-year prospective study. Journal of Dentistry (2014), http://dx.doi.org/10.1016/j.jdent.2014.03.008

21. Casap N, Zeltser C, Wexler A, Tarazi E, Zeltser R. Immediate placement of dental implants into debrided infected dentoalveolar sockets. *Journal of Oral and Maxillofacial Surgery* 2007;**65**:384–92.
22. Schoop U, Barylyak A, Goharkhay K, Beer F, Wernisch J, Georgopoulos A, *et al*. The impact of an erbium, chromium:yttrium–scandium–gallium–garnet laser with radial-firing tips on endodontic treatment. *Lasers in Medical Science* 2009;**24**:59–65.
23. Kusek RE. Immediate implant placement into infected sites: bacterial studies of the Hidroacoustic effects of the YSGG laser. *Journal of Oral Implantology* 2011;**37 Spec. No.**:205–11.
24. Oyagüe RC, Turrión AS, Toledano M, Monticelli F, Osorio R. In vitro vertical misfit evaluation of cast frameworks for cement-retained implant-supported partial prostheses. *Journal of Dentistry* 2009;**37**:52–8.
25. Oyagüe RC, Sánchez-Turrión A, López-Lozano JF, Suárez-García MJ. Vertical discrepancy and microleakage of laser-sintered and vacuum-cast implant-supported structures luted with different cement types. *Journal of Dentistry* 2012;**40**:123–30.
26. Montero J, Manzano G, Beltrán D, Lynch CD, Suárez-García MJ, Castillo-Oyagüe R. Clinical evaluation of the incidence of prosthetic complications in implant crowns constructed with UCLA castable abutments. A cohort follow-up study. *Journal of Dentistry* 2012;**40**:1081–9.
27. Gómez-Cogolludo P, Castillo-Oyagüe R, Lynch CD, Suárez-García MJ. Effect of electric arc, gas oxygen torch and induction melting techniques on the marginal accuracy of cast base-metal and noble metal-ceramic crowns. *Journal of Dentistry* 2013;**41**:826–31.
28. Castillo-Oyagüe R, Osorio R, Osorio E, Sánchez-Aguilera F, Toledano M. The effect of surface treatments on the microroughness of laser-sintered and vacuum-cast base metal alloys for dental prosthetic frameworks. *Microscopy Research and Technique* 2012;**75**:1206–12.
29. Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: a review and proposed criteria of success. *International Journal of Oral and Maxillofacial Implants* 1986;**1**:11–25.
30. Gatti C, Chiapasco M. Immediate loading of Brånemark implants: a 24-month follow-up of a comparative prospective pilot study between mandibular overdentures supported by Conical transmucosal and standard MK II implants. *Clinical Implant Dentistry and Related Research* 2002;**4**:190–9.
31. Crespi R, Capparè P, Gherlone E. Fresh socket implants in periapical infected sites in humans. *Journal of Periodontology* 2010;**81**:378–83.
32. Hannigan A, Lynch CD. Statistical methodology in oral and dental research: pitfalls and recommendations. *Journal of Dentistry* 2013;**41**:385–92.
33. Karoussis IK, Salvi GE, Heitz-Mayfield LJ, Brägger U, Hämmerle CH, Lang NP. Long-term implant prognosis in patients with and without a history of chronic periodontitis: a 10-year prospective cohort study of the ITI Dental Implant System. *Clinical Oral Implants Research* 2003;**14**:329–39.
34. Tonetti M, Palmer R, Working Group 2 of the VIII European Workshop on Periodontology. Clinical research in implant dentistry: study design, reporting and outcome measurements: consensus report of Working Group 2 of the VIII European Workshop on Periodontology. *Journal of Clinical Periodontology* 2012;**39**:73–80.
35. Álvarez-Camino JC, Valmaseda-Castellón E, Gay-Escoda C. Immediate implants placed in fresh sockets associated to periapical infectious processes. A systematic review. *Medicina Oral Patología Oral y Cirugía Bucal* 2013;**18**:780–5.
36. Mura P. Immediate loading of tapered implants placed in postextraction sockets: retrospective analysis of the 5-year clinical outcome. *Clinical Implant Dentistry and Related Research* 2012;**14**:565–74.
37. Blus C, Szmukler-Moncler S, Khoury P, Orrù G. Immediate implants placed in infected and noninfected sites after atraumatic tooth extraction and placement with ultrasonic bone surgery. *Clinical Implant Dentistry and Related Research* 2013. http://dx.doi.org/10.1111/cid.12126. [in press].
38. Koch GG, Paquette DW. Design principles and statistical considerations in periodontal clinical trials. *Annals of Periodontology* 1997;**2**:42–63.
39. Corbella S, Taschieri S, Tsesis I, Del Fabbro M. Postextraction implant in sites with endodontic infection as an alternative to endodontic retreatment: a review of literature. *Journal of Oral Implantology* 2013;**39**:399–405.
40. Sundqvist G. Associations between microbial species in dental root canal infections. *Oral Microbiology and Immunology* 1992;**7**:257–62.
41. Peters LB, Wesselink PR, van Winkelhoff AJ. Combinations of bacterial species in endodontic infections. *International Endodontic Journal* 2002;**35**:698–702.
42. Keller U, Hibst R. Experimental studies of the application of the Er:YAG laser on dental hard substances: II. Light microscopic and SEM investigations. *Lasers in Surgery and Medicine* 1989;**9**:345–51.
43. Coleton SH. The use of lasers in periodontal therapy. *Alpha Omegan* 2008;**101**:181–7.
44. Del Fabbro M, Boggian C, Taschieri S. Immediate implant placement into fresh extraction sites with chronic periapical pathologic features combined with plasma rich in growth factors: preliminary results of single-cohort study. *Journal of Oral and Maxillofacial Surgery* 2009;**67**:2476–84.
45. Novaes Jr AB, Novaes AB. Immediate implants placed into infected sites: a clinical report. *International Journal of Oral and Maxillofacial Implants* 1995;**10**:609–13.
46. Villa R, Rangert B. Early loading of interforaminal implants immediately installed after extraction of teeth presenting endodontic and periodontal lesions. *Clinical Implant Dentistry and Related Research* 2005;**7**:S28–35.
47. Novaes Jr AB, Marcaccini AM, Souza SL, Taba Jr M, Grisi MF. Immediate placement of implants into periodontally infected sites in dogs: a histomorphometric study of bone-implant contact. *International Journal of Oral and Maxillofacial Implants* 2003;**18**:391–8.
48. Liljenqvist U, Lerner T, Bullmann V, Hackenberg L, Halm H, Winkelmann W. Titanium cages in the surgical treatment of severe vertebral osteomyelitis. *European Spine Journal* 2003;**12**:606–12.
49. Addy LD, Lynch CD, Locke M, Watts A, Gilmour AS. The teaching of implant dentistry in undergraduate dental schools in the United Kingdom and Ireland. *British Dental Journal* 2008;**205**:609–14.
50. Preciado A, Del Río J, Lynch CD, Castillo-Oyagüe R. A new, short, specific questionnaire (QoLIP-10) for evaluating the oral health-related quality of life of implant-retained overdenture and hybrid prosthesis wearers. *Journal of Dentistry* 2013;**41**:753–63.
51. Preciado A, Del Río J, Lynch CD, Castillo-Oyagüe R. Impact of various screwed implant prostheses on oral health-related quality of life as measured with the QoLIP-10 and OHIP-14 scales: a cross-sectional study. *Journal of Dentistry* 2013;**41**:1196–207.

UNCORRECTED PROOF

Please cite this article in press as: Torres-Sánchez DTDDIFFDC, et al. Outcome of single immediate implants placed in post-extraction infected and non-infected sites, restored with cemented crowns: A 3-year prospective study. Journal of Dentistry (2014), http://dx.doi.org/10.1016/j.jdent.2014.03.008