ORIGINAL RESEARCH

Wound Healing in Dental Implant Surgery in Patients with or without Antibiotic Prophylaxis

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ABSTRACT

Aim: To assess the association of various clinical parameters and proinflammatory cytokines in the wound-healing process of dental implants with the presence or absence of antibiotic prophylaxis.

Materials and methods: The present study included evaluation of early wound-healing process in patients undergoing dental implant placement procedures with and without antibiotic prophylaxis. A total of 50 patients with partial edentulous arch were included in the present study. All the subjects were broadly divided into two study groups depending upon the presence or absence of prophylactic antibiotic therapy, with 25 patients in each group. One group consisted of subjects who were given prophylactic amoxicillin (2 gm), 1 hour before the starting of the surgery, followed by 500 mg 3 times a day for 1 week. Detection of interleukin (IL)-1β and -8 cytokine levels in the gingival crevicular fluid (GCF)/peri-implant crevicular fluid (PICF) was done immediately after the dental surgery. All the results were compiled and analyzed by Statistical Package for the Social Sciences (SPSS) software version 17.0.

Results: A significant increase in the PICF IL-1β concentration at postoperative follow-up time was observed in the antibiotic group in comparison with the baseline values. A significant increase in the IL-8 concentration postoperatively in comparison with the baseline values in the antibiotic group was also observed. At the time of surgery, the IL-8 concentrations were statistically lower in the antibiotic group in comparison with the other study group. Concentration of amoxicillin, as observed by high-performance liquid chromatography (HPLC), was lower than the minimum detection levels.

Conclusion: Detection of amoxicillin is not feasible within the GCF samples immediately after dental surgery procedure.

Clinical significance: Clinical usefulness of prophylactic use of amoxicillin is still doubtful.

Keywords: Amoxicillin, Antibiotic prophylaxis, Cytokines, Dental implant.

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INTRODUCTION

In the present scenario of dentistry, the main aim of a dentist is the preservation of the oral health of patient and to achieve healthy contour, comfort, function, speech, etc. Dental implant is one of the most preferred lines of treatment for patients undergoing prosthetic rehabilitation of missing teeth.[1] However, failure rates have also been reported in the past literature in relation to dental implants. Development of bacteremia around dental implants is one of the major reasons for the failure of dental implants. Once infected, replacement of dental implants has to be done when visualized from prognostic point of view. Usually, infectious endocarditis is one of the few conditions in which antibiotic prophylaxis is given in patients scheduled to undergo surgical procedures, including dental implant surgery.[2,3]

For minimizing infections after implant placement in the dental arches, different antibiotic prophylactic systems have been proposed from time to time. Short-term antibiotic prophylaxis has been advocated by various authors in the recent past. However, the practice of antibiotics prophylaxis in implant dentistry is still a topic of debate.[3,4]

Gingival crevicular fluid is a compound mixture of elements obtained from serum, host tissues, and structural cells of the periodontal tissue, along with oral bacteria.[5] In patients undergoing specific therapy, including dental implant procedures, GCF and PICF might be used, as they basically become wound fluids. Proinflammatory cytokines IL-1β and IL-8 have been evaluated in GCF/PICF for assessing their role as potential diagnostic indicators for periodontal and peri-implant health.[6-8]

Under the light of above-mentioned data, the present study was planned to assess the efficacy of GCF and PICF samples obtained from surgical dental implant sites in evaluating early changes around the same implants, after 1 week of healing. The association of various clinical parameters and proinflammatory cytokines in the wound-healing process of dental implants with the presence or absence of antibiotic prophylaxis was also instigated.

MATERIALS AND METHODS

The present study was designed in the Department of Oral Implantology of the dental institute and it included evaluation of early wound-healing process in patients undergoing dental implant placement procedures with and without antibiotic prophylaxis. Ethical approval was obtained from the ethical committee of the institution. Written consent was also obtained from all the patients after explaining in detail the entire research protocol. Inclusion criteria for the present study included:

- Patients between the ages of 20 and 50 years,
- Patients with missing permanent mandibular first molar and had planned to undergo prosthetic rehabilitation for the same by single dental implant,
- Patients with absence of any type of systemic illness,
- Patients with intact healthy adjacent teeth, and
- Patients with absence of any known drug allergy.

After meeting the inclusion criteria, a total of 50 patients with partial edentulous arch were included in the present study, which were scheduled to undergo prosthetic rehabilitation by one-stage dental implant procedure. All the subjects were broadly divided into two study groups, depending upon the presence or absence of prophylactic antibiotic therapy, with 25 patients in each group. One group consisted of subjects who were given prophylactic amoxicillin (2 gm), 1 hour before the starting of the surgery, followed by 500 mg 3 times a day for 1 week, based on the criteria described previously in the literature.[9] The other group consisted of subjects who did not receive antibiotic prophylaxis (control group). Follow-up record of the patient was done on 7th day postoperatively. Standard surgical procedure, as per manufacturer's recommendations, was used for placing the dental implants. Removal of sutures was done after 1 week postoperatively. For reaching a definite periodontal diagnosis, the following parameters were checked: Probing depth, gingival recession, level of clinical attachment, involvement of furcation and mobility of tooth, based on the criteria described previously in literature.[10] Single experienced examiner was appointed for obtaining the plaque index (PI) and gingival index (GI), using four tooth/implant surfaces.[11,12] This was done initially prior to the surgery and repeated 1 week after insertion of the dental implants. In the immediate time prior to the surgery, GCF samples were obtained for the determination of cytokine levels. However, for the determination of local amoxicillin levels, GCF samples immediately after the surgical procedure were obtained. One week postoperatively, before removing the sutures, we obtained the PICF samples from the newly forming peri-implant crevice. Isolation and drying of the gingival tissue were done with cotton rolls followed by gentle steam of air. A sterile paper filter strip was used for the collection of GCF and PICF. An electronic quantification unit was used for measuring the GCF/PICF volume. Sterile vials without buffer were used for the placement of strips designated for HPLC assay.[13] Sample collection was done from four sites per tooth or dental implant for assessing PI and GI. An enzyme reaction buffer solution containing 50 mm Tris–HCl, 0.2 M NaCl, and $CaCl_2$ was used for placement of strips which were assigned for enzyme-linked immunosorbent assay (ELISA).[14]

Immediately after the dental implant surgery, peripheral blood samples were taken from the subjects who were given amoxicillin. A 5 mL vial was used for collecting the blood samples drawn from the patients. All the vials were stored overnight at 4°C. For the detection of IL-1β and -8 cytokine levels in the GCF/PICF, commercial available ELISA kit (Cytokine ELISA kits, Biogene, India) was used; 3.5 and 1 pg/mL were the minimum detectable concentration for IL-8 and IL-1β respectively. Cytokine concentrations were evaluated by utilizing a dilution factor for every cytokine for a specific plate and changed back into a concentration derived from the originally collected total GCF/PICF volume. Detection of amoxicillin was done by absorbance at 227 nm. For the recognition of the amoxicillin concentrations, modification of the HPLC method, as described by Tenenbaum et al,[15] was used. Deproteinization of the 200-µL serum

samples was done with equal amount of acetonitrile. This was followed by centrifugation of the samples for the recovery of the supernatant. Addition of methylene chloride was done to this supernatant obtained, followed by mixing of the samples by rotation, for 10 minutes at 20 rpm. In the HPLC instrument, 10 μL of this aliquot was injected. Extraction of the GCF samples was done, followed by addition and mixing of methylene chloride. Centrifugation of the mixture was done followed by collection of the final upper aqueous layer; 2.5 ng was the detection limit for amoxicillin. Analysis of amoxicillin level was done immediately postoperatively and after 1 week. For analysis of all the results, SPSS software version 17.0 was used. Chi-square test, Mann–Whitney U test and univariate regression curve were used for the assessment of level of significance. A p-value of less than 0.05 was taken as significant.

RESULTS

In the present study, the mean age of the subjects of the antibiotic group and the control group was 42.5 and 45.1 years respectively, as shown in Table 1. Noris Medical dental implant systems were the most common type of dental implants used in the present study, seen to be present in 17 and 14 patients of antibiotic group and control group respectively, as shown in Graph 1. Mean GI

Table 1: Demographic and dental implant characteristics among patients of the present study

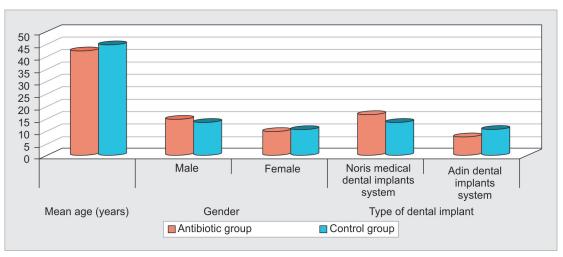| Parameter		Antibiotic group	Control group
Mean age (years)		42.5	45.1
Gender	Male	15	14
	Female	10	11
Type of dental implant	Noris medical dental implant system	17	14
	Adin dental implant systems	8	11

values of the subjects in the antibiotic group at baseline level and at 1 week postoperatively were 0.91 and 0.84 respectively. Mean GI values of the subjects in the control group at baseline level and at 1 week postoperatively were 0.88 and 1.19 respectively, as shown in Table 2. Mean IL-1β values in the antibiotic group patients and in the control group patients at 1 week postoperatively were 410 and 458 pg/mL respectively. Mean IL-8 levels among the patients of the antibiotic group and the control group at 1 week postoperatively were 4415 and 3525 pg/mL respectively, as shown in Graph 2.

A significant increase in the PICF IL-1β concentration at postoperative follow-up time was observed (p-value <0.05). It was observed that there was a significant increase in the IL-8 concentration postoperatively in
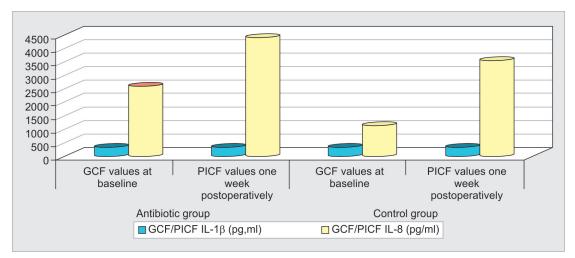
Table 2: Comparison of clinical parameters and cytokine concentrations during early wound-healing phase

Parameter	Antibiotic group		Control group		p-value of alteration in the parameter (overall)
	GCF values at baseline	PICF values 1 week postoperatively	GCF values at baseline	PICF values 1 week postoperatively	
GI	0.91	0.84	0.88	1.19	0.02*
PI	0.92	0.93	0.88	1.15	0.01*
GCF/PICF volume (μL)	6.6	6.2	7.1	7.2	0.52
GCF/PICF IL-1β (pg/mL)	310	410	305	458	0.03*
GCF/PICF IL-8 (pg/mL)	2540	4415	1102	3525	0.01*

*Significant

Graph 1: Clinical and demographic details of dental implants

Graph 2: Clinical parameters and cytokine concentrations during early wound-healing phase

comparison with the baseline values in the antibiotic group. At the time of surgery, the IL-8 concentrations were statistically lower in the antibiotic group in comparison with the other study group (p-value < 0.05). Concentration of amoxicillin, as observed by HPLC, in the study group at immediate postoperative time and after 1 week of follow-up was found to be 13.25 and 10.25 μg/mL, which were found to be statistically significant.

DISCUSSION

Whether antibiotic prophylaxis should be used in all the patients undergoing dental implant procedures is still a topic of current discussion. Use of 0.2% chlorhexidine rinsing solution before treatment protocol might be a clinically relevant option in patients undergoing dental implant surgeries. There is a high risk of dental implant failure in subjects in whom dental implant gets infected. Therefore, for the prevention of infection at the dental implant site, prophylactic antibiotic therapy is prescribed for reducing the chance of bacterial proliferation and infection. Dentistry still lacks accurate guidelines for antibiotic prophylaxis in strict sense.[14-16] Hence, the correlation of various clinical parameters and proinflammatory cytokines in the wound-healing process of dental implants with the presence or absence of antibiotic prophylaxis was evaluated.

A total of 50 patients were evaluated in the present study and broadly divided into two study groups: Antibiotic group and the control group, as shown in Table 1 and Graph 1. The collection of PICF samples 1 week after the dental implant placement was feasible, along with detection of other biomarkers. We observed modest effect of amoxicillin on different clinical periodontal parameters during 1st week postoperatively after dental implant placement. In our study, postoperative values of PI were higher because of absence of mechanical cleansing of

the surgical sites, as advised by the implantologists. A transient rise in the GI values during 1st week of postoperative healing was observed in the present study, which could be attributed to physiologic inflammatory response. While comparing the total crevicular fluid volume per tooth and per implant at first postoperative appointment, no significant results were obtained. Our results were in concordance with the results obtained by previous authors who have reported a positive association between crevicular fluid production and clinicopathologic signs of inflammation around teeth or dental implants.[16,17]

A rise in IL-1β and IL-8 PICF concentrations during the first postoperative week after placement of dental implants in comparison with the baseline GCF value was also observed. The values were statistically significant for both the study groups. While assessing the HPLC readings, values of amoxicillin were too low to be detected. Therefore, the efficacy of amoxicillin is questionable when prescribed for preventing the adverse effects of bacterial contamination around dental implant healing tissue. In one of the previous studies conducted by Dent et al[18] involving 2,641 dental implants, the authors observed significantly lesser failure rates in patients in which preoperative antibiotic were prescribed.

Nowzari et al[19] highlighted the levels of selected proinflammatory cytokines in patient with clinically healthy peri-implant and periodontal sites, and examined the role and correlation of cytokine to specific bacterial/viral pathogens. They evaluated a total of 11 subjects, with a mean age of 56.2 years in their study. They obtained subgingival microbiological samples and cultured them for assessing the growth of periodontopathic bacteria. They analyzed the GCF samples for checking the presence of human cytomegalovirus (HCMV) and other inflammatory markers, using flow cytometry (fluorescence-activated cell sorter). In areas around dental

implants, they observed higher prevalence and levels of periodontopathic bacteria. Also, in comparison with the teeth, a higher concentration of cytokines was observed by the authors around the dental implant sites. However, they did not detect any HCMV in their study. Authors from one of the previous studies evaluated the cytokine levels in the GCF of patients around dental implants with ceramic and titanium abutments. They showed that levels of IL-1β and IL-6 in the GCF around ceramic abutments were significantly lower in comparison with titanium implants.[20] Abdulwassie and Dhanrajani[21] analyzed patients undergoing dental implant procedures in a retrospective study. They prescribed amoxicillin to all the patients and carried it for 10 days postoperatively. A high success rate of approximately 95% was achieved in their study. Sharaf et al,[22] in one of the previous studies, assessed the failure rate of dental implants in subjects who were prescribed perioperative antibiotic therapy, in comparison with those who were not. From the results, the authors concluded that a single dose of antibiotic therapy when given preoperatively might marginally decrease the failure rate of dental implants.

In another study conducted by Surapaneni et al[23] on the bacteria present in peri-implantitis patients, authors observed that a variety of bacteria were present in the samples taken from peri-implant tissue and concluded that inflammatory lesions around dental implants and adult periodontitis patients had approximately similar microbial flora. Therefore, the success of dental implants also depends upon the maintenance of sterile surgical field. This can be done by using antiseptic mouthwashes, thorough irrigation of the wound, or by doing presurgical surgical rinse. Reduction in the dental implant loss up to 10% has been reported by immediate preoperative use of 0.12% of chlorhexidine mouthwash.[24] Most of the dentists prefer prescribing antibiotics before dental implant procedures as a precautionary measure. In one of the past studies, it was shown that about two-fifths of dentists prefer prescribing antibiotics in the absence of relevant medical history.[25]

CONCLUSION

Success of dental implants is largely dependent upon the level of sterilization and disinfection maintained during the surgical procedure. Shortly after the initial oral dose, amoxicillin could be detected in the peripheral blood samples. However, immediately after the single-stage dental implant surgery, detection of amoxicillin within GCF is not feasible. Average modest effect of amoxicillin prophylaxis seems to be present on the clinical periodontal parameters. Hence, we recommend further studies in this area for better exploration of this field of antibiotics and dental implant.

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